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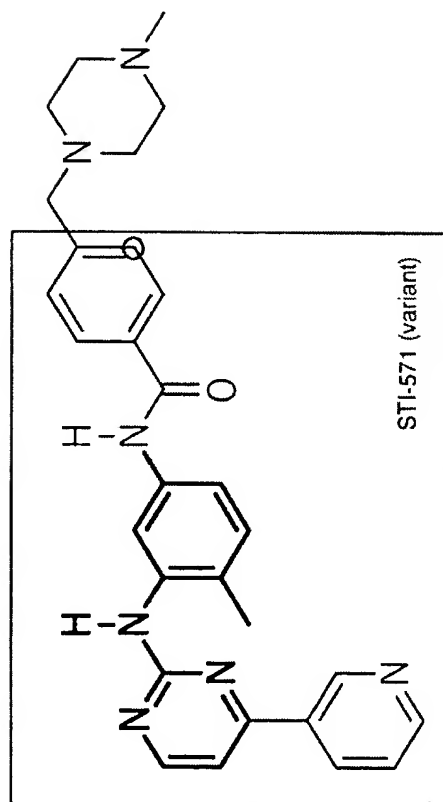
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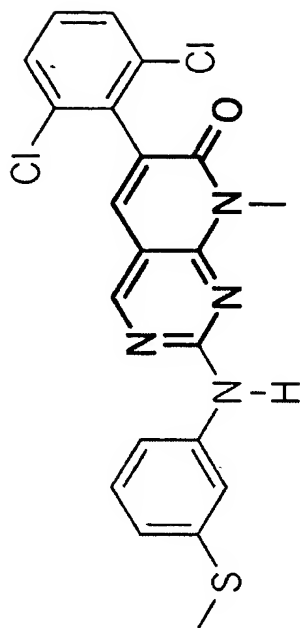
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STI-571



PD173955

Figure 1

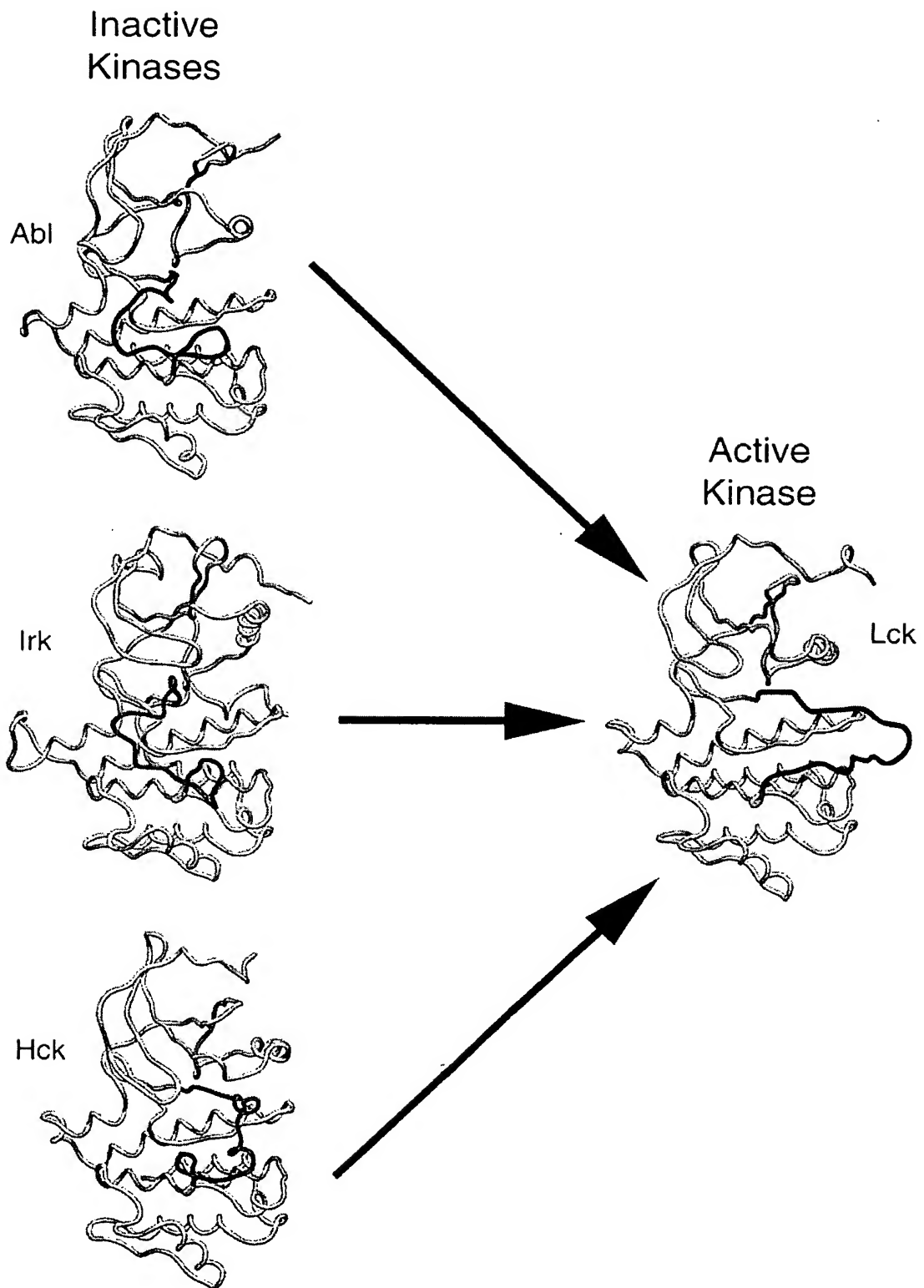


Figure 2

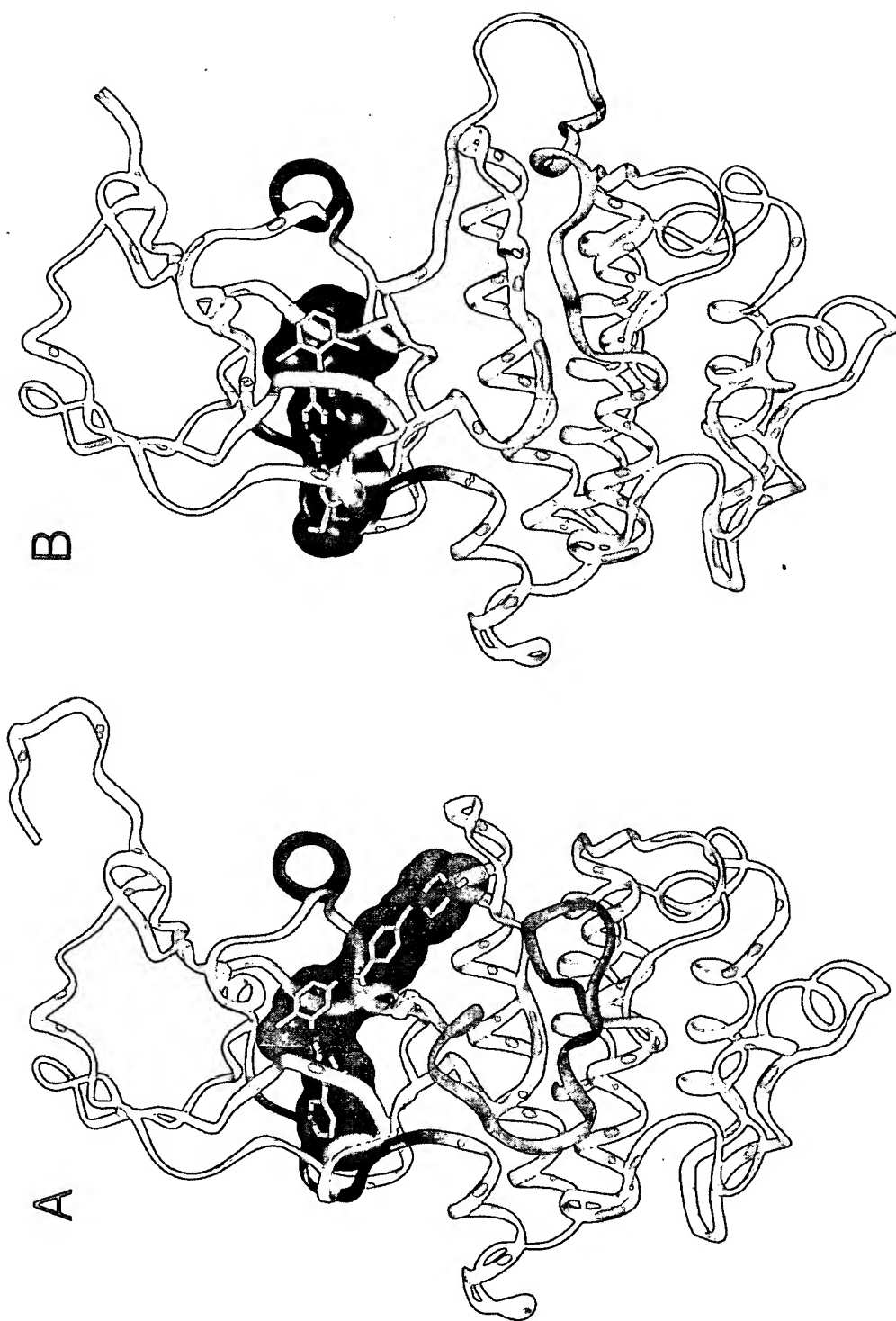
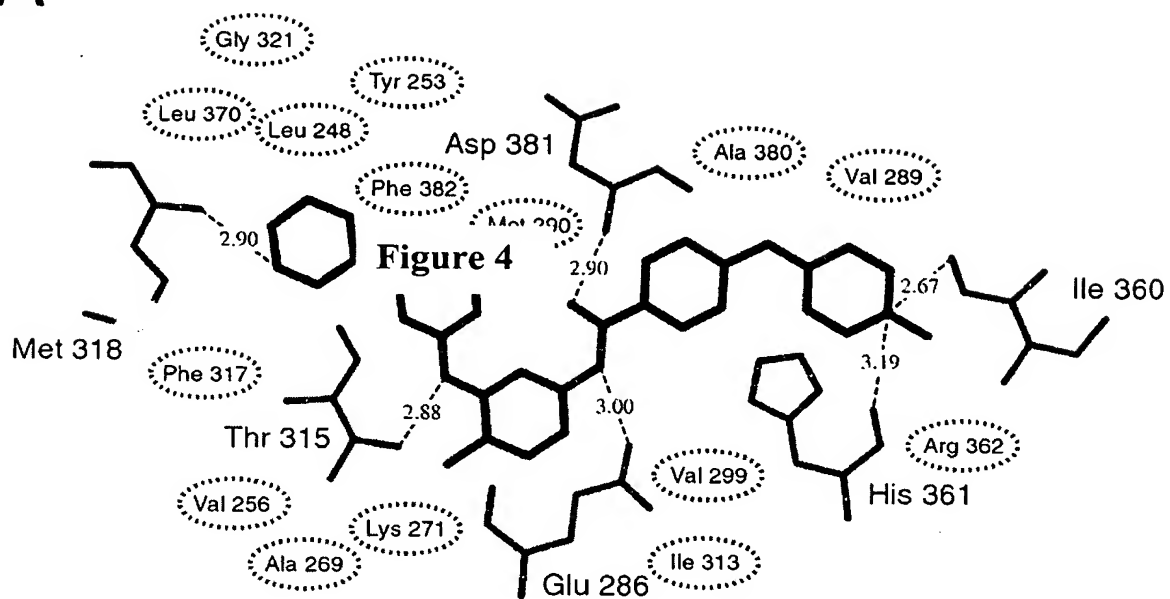


Figure 3

A



B

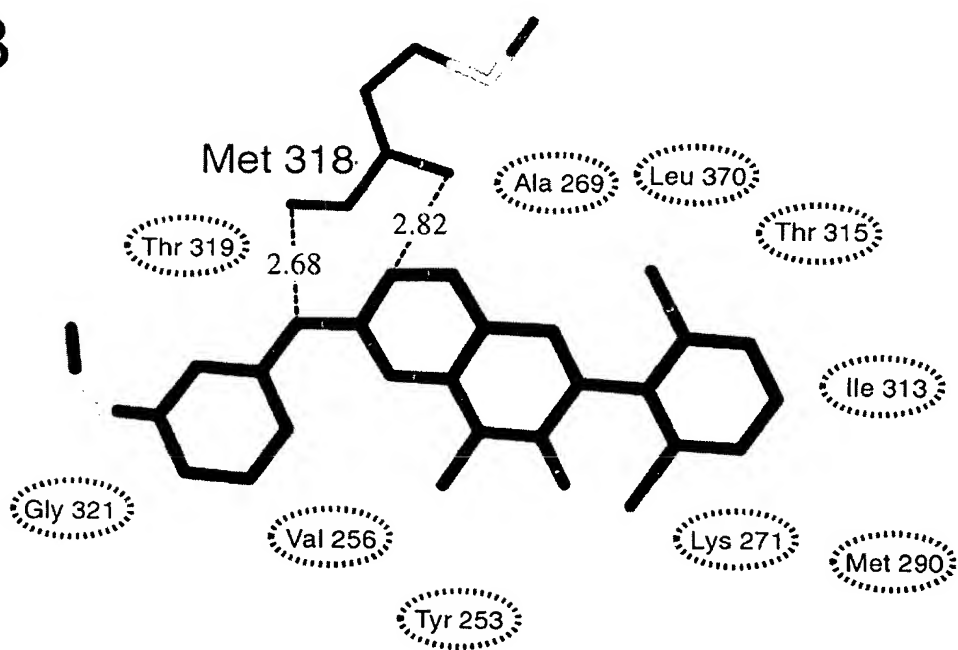


Figure 4

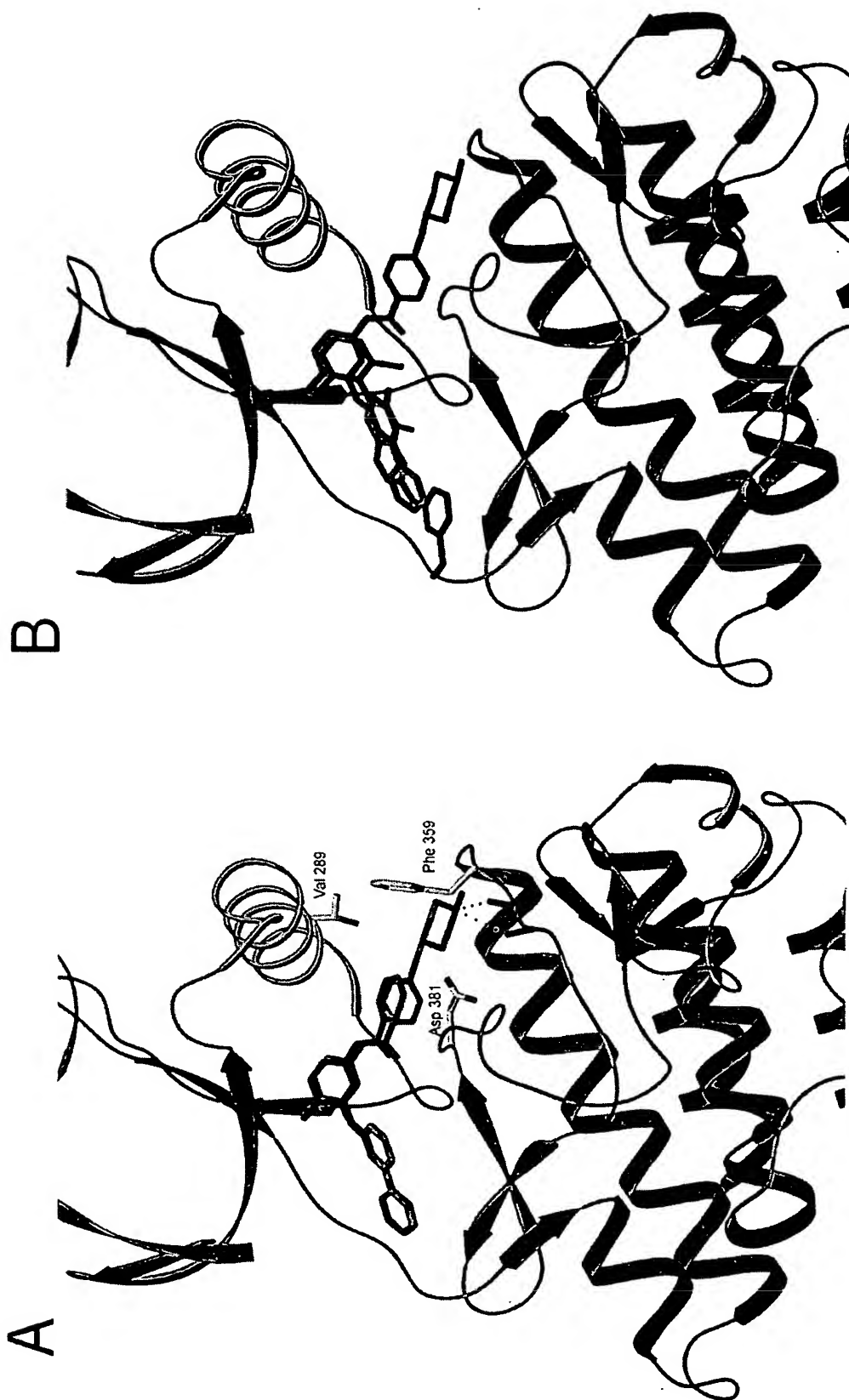


Figure 5

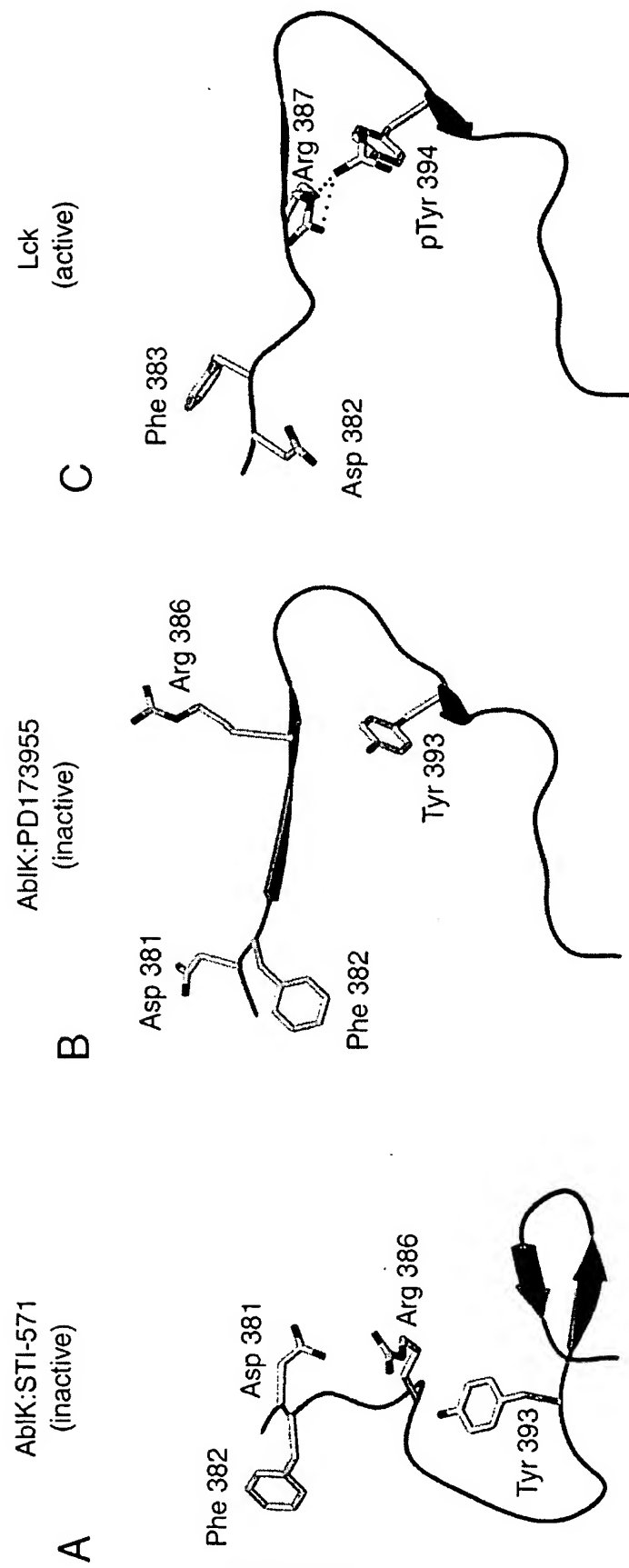


Figure 6

A



B

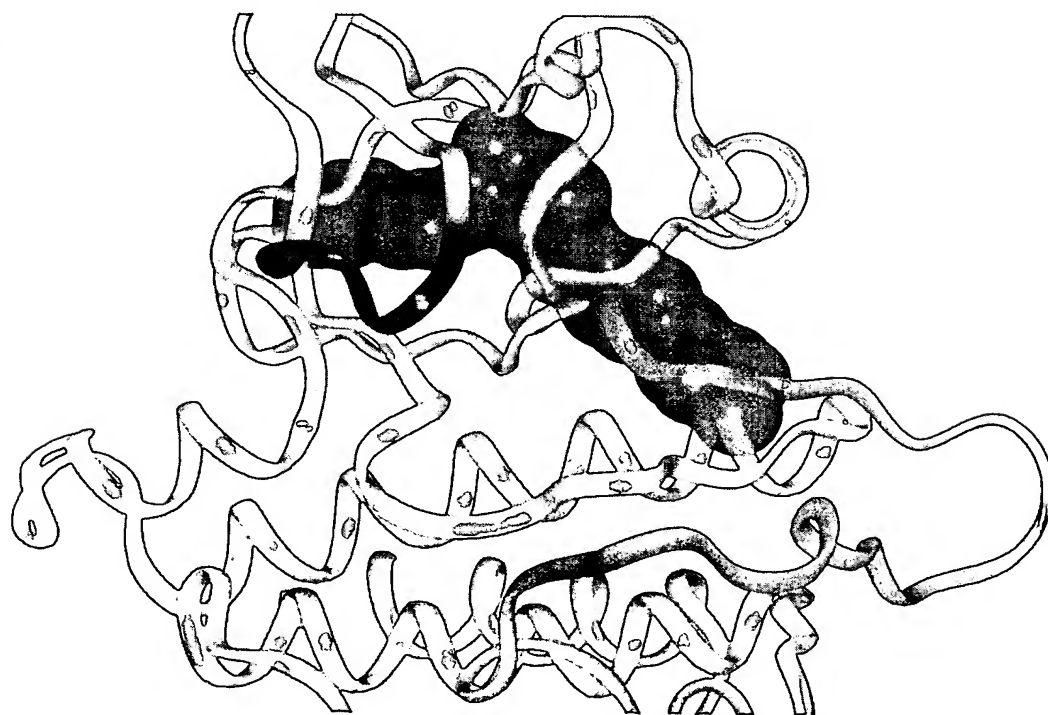
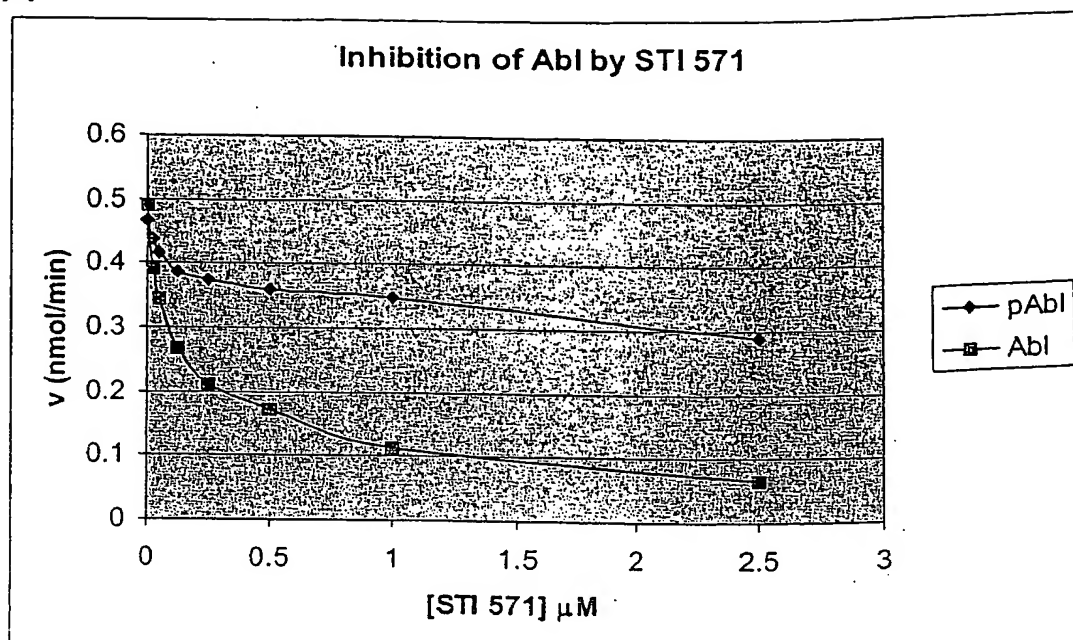


Figure 7

A



B

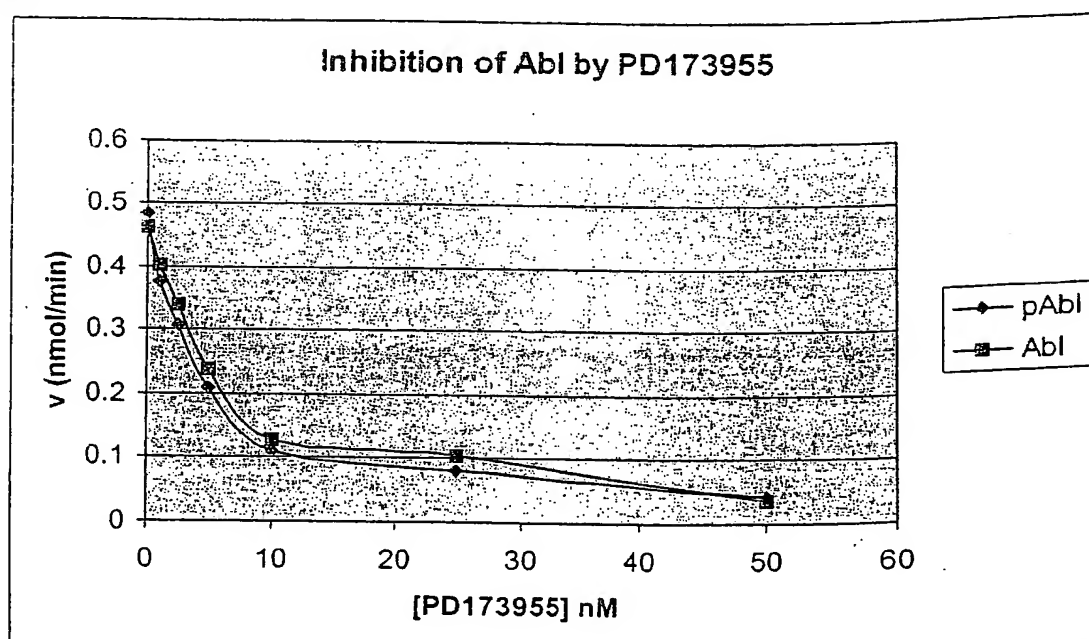
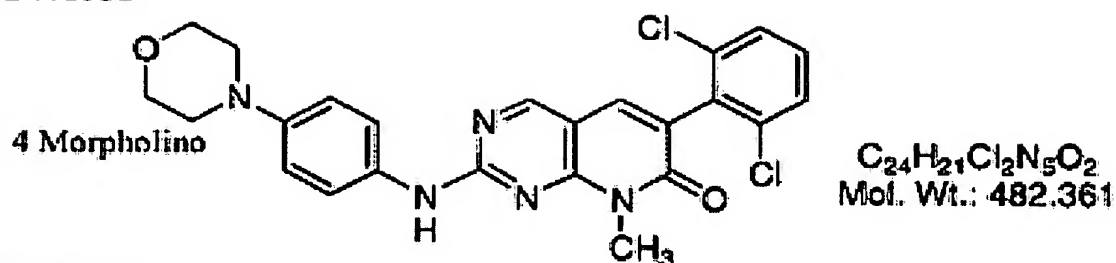
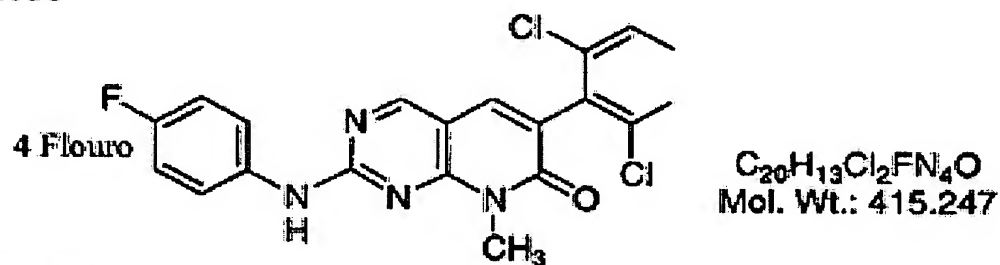


Figure 8

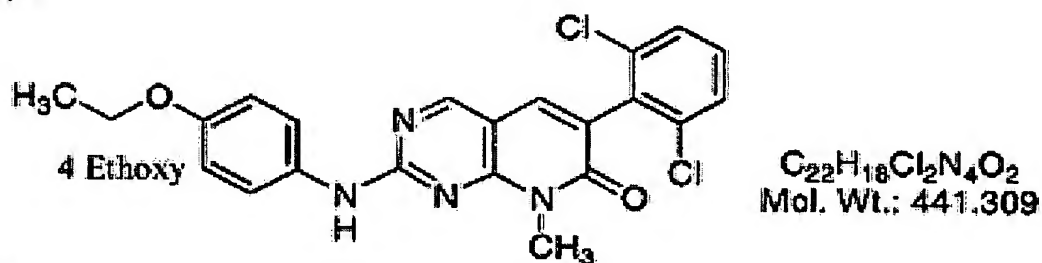
PD173952



PD173956



PD173958



PD166326

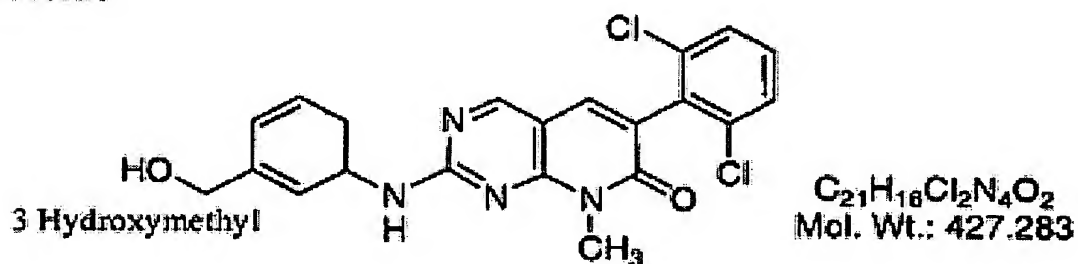


Figure 9

Comparative Inhibition of Growth of R10 NEG Cells in Liquid Culture by STI571 (5 - 500 nM), PD173955 (0.5 - 50 nM), & PD166326 (0.1 - 10 nM)

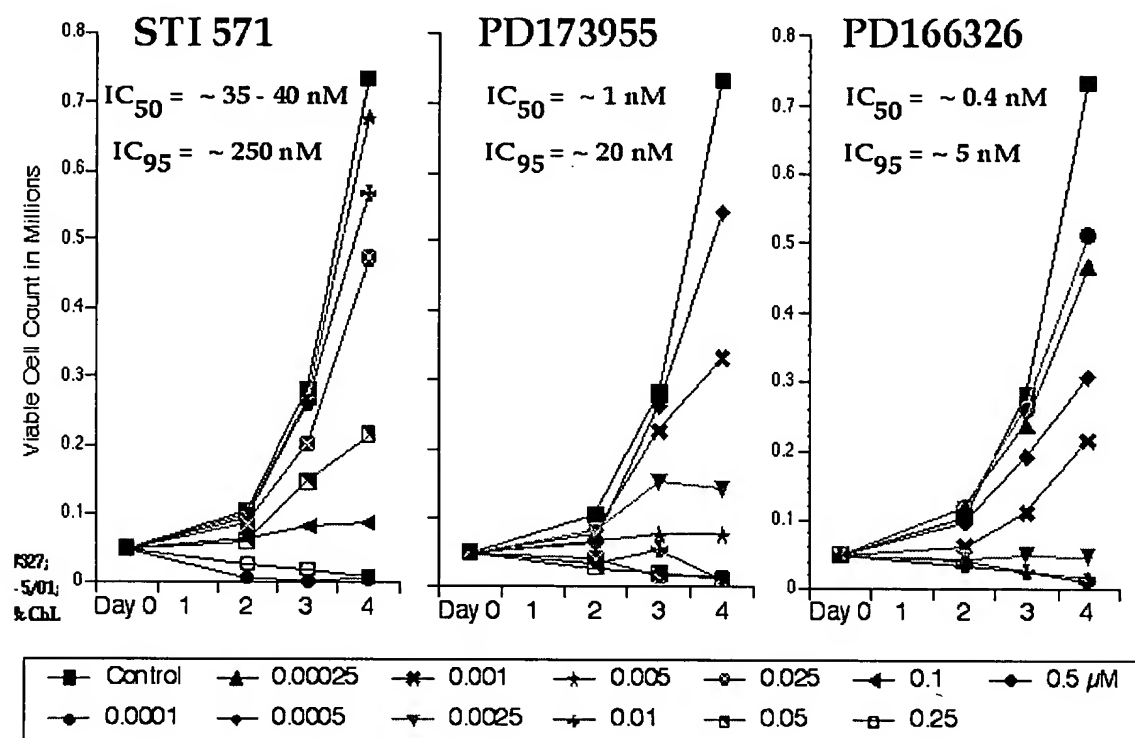


Figure 10

Inhibition of ^3H -Tdr Uptake in Fresh Blast Cells from CML Patient in Blastic Phase by STI571, PD173955, & PD166326

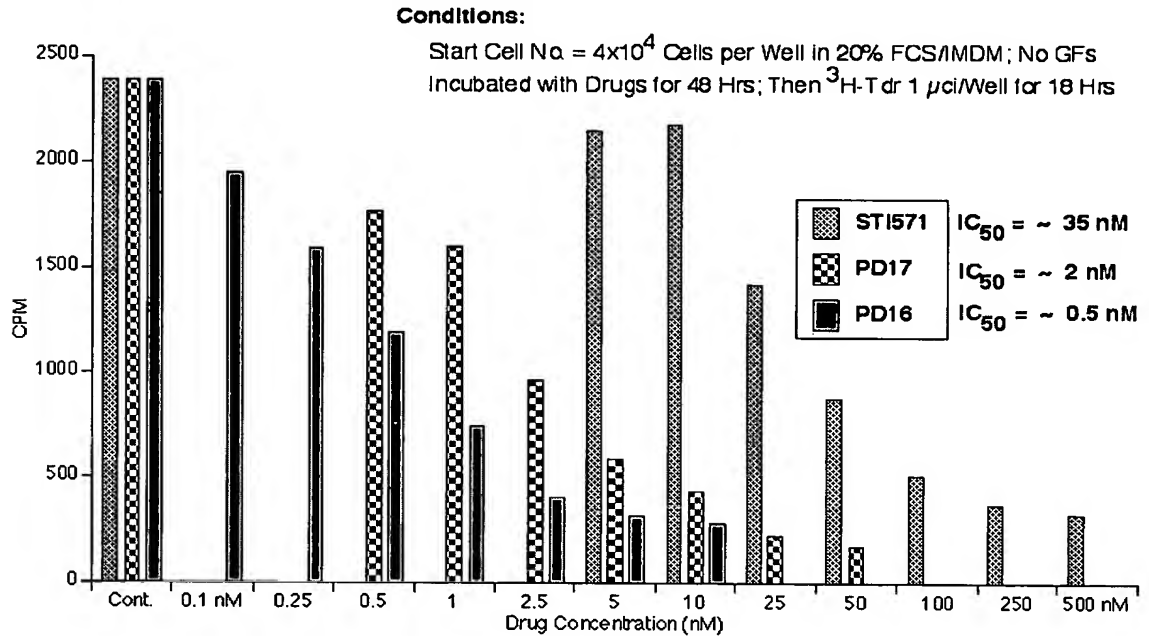


Figure 11

Inhibition of ^3H -Tdr Uptake by Fresh Blast Cells with & without Cytokines from the Same CML Patient in Blastic Phase by STI571, PD173955, & PD166326

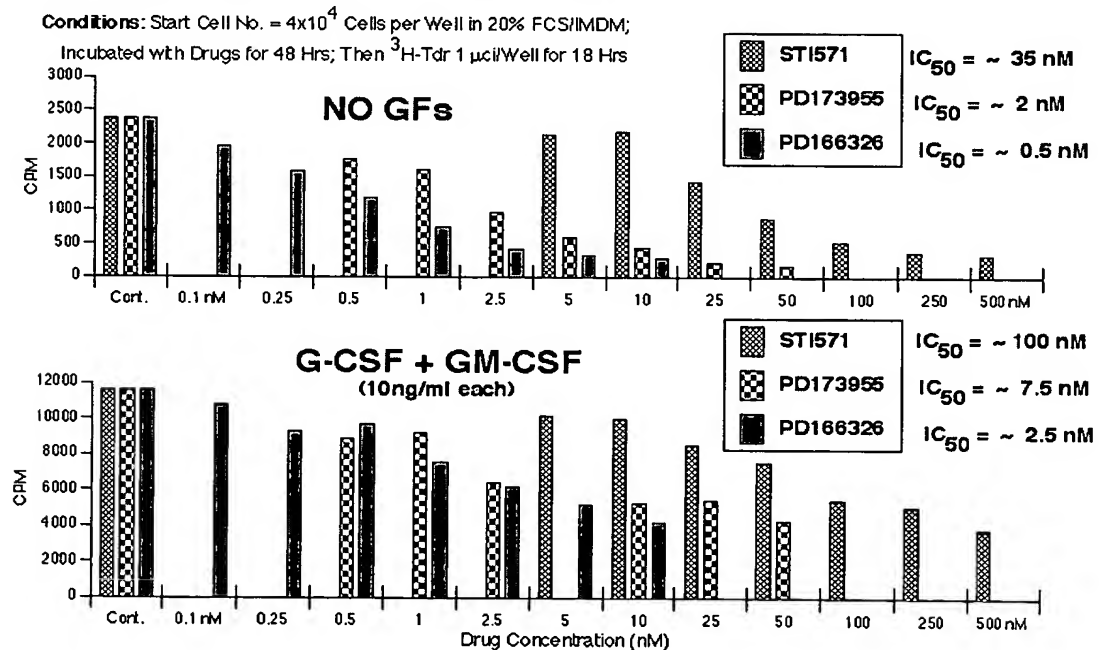


Figure 12

Relative Sensitivity of Various Human Tumor Cell Lines to PD173955

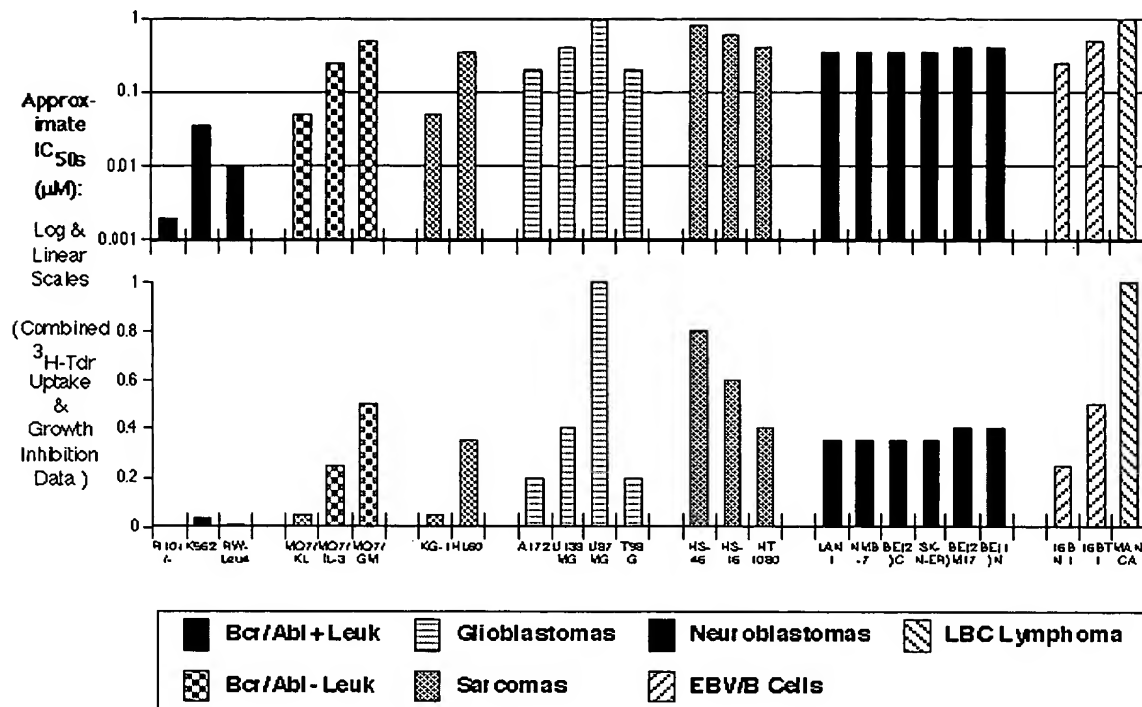


Figure 13

Relative Sensitivity of Various Human Tumor Cell Lines to PD173955 & STI571

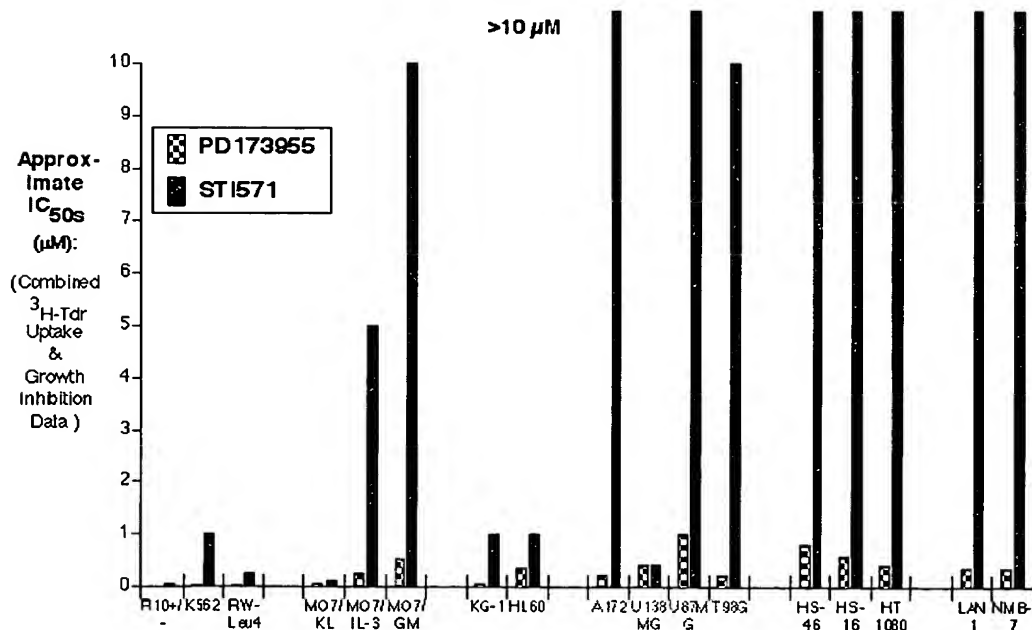


Figure 14

PD 166326 binding to Abl Kinase (Modelled)

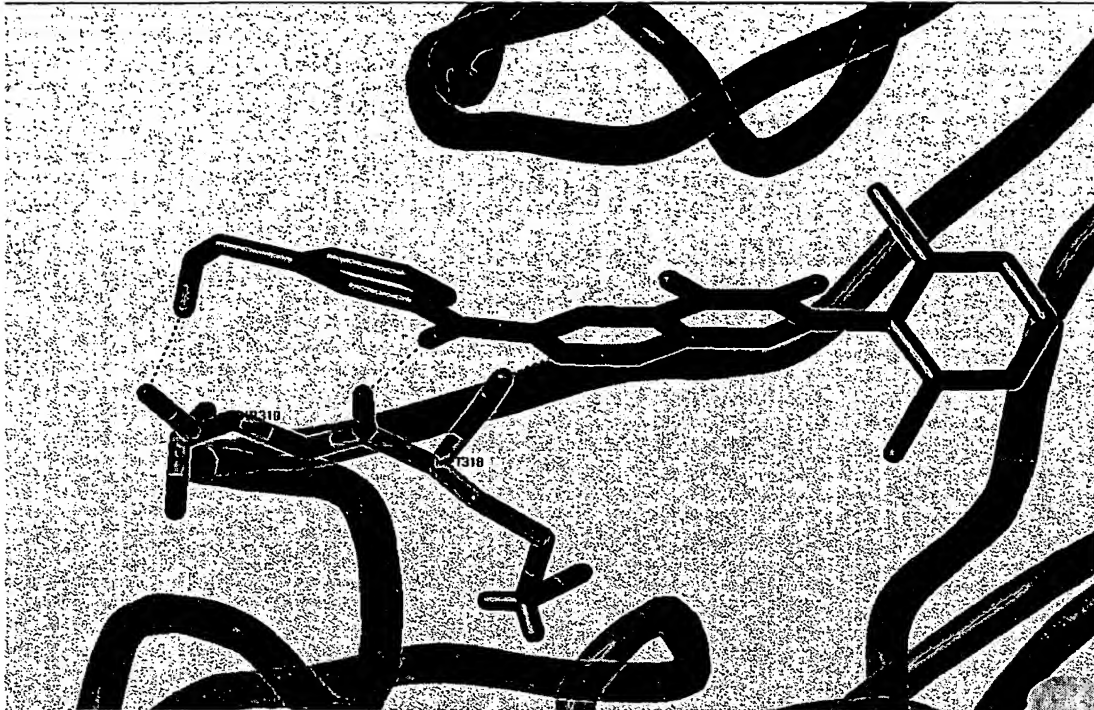


Figure 15

10 nM PD173955 Inhibits Primary Early CML CD34+ GM Progenitors (0 - 5 Days) Substantially More than Later Maturing Progenitors (4 - 8 Days); No Inhibition of Comparable Normal Progenitors (Mean Values 3 Experiments)

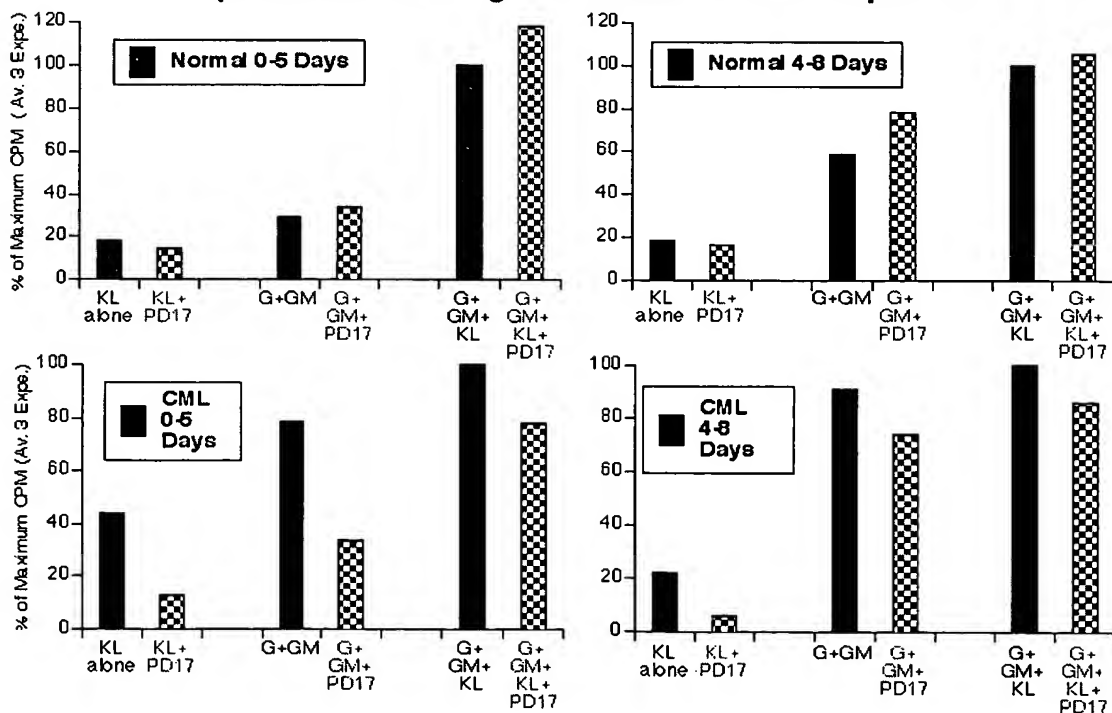
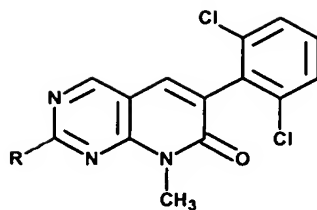


Figure 16

| | IC50 (nM) | IC95-99 (nM) |
|----------------------------|-----------|--------------|
| PD166326 | 0.4 | 2.5 |
| SKI DV MO-16 | 0.5 | 3.5 |
| SKI DV MO-17 | 0.6 | 7.5 |
| SKI DV2 43 | 0.8 | 7.5 |
| SKI DV1 10 | 0.8 | 10 |
| Biotinyl SKI DV1 10 | 1.5 | 10 |
| SKI DV2 47 | 1.5 | 10 |
| SKI DV 115 | 2 | 10 |
| SKI DV2 51 | 2.5 | 15 |
| SKI DV2 87 | 2.5 | 20 |
| SKI DV2 37 | 7.5 | 50 |
| SKI DV2 53 | 15 | 100 |
| SKI DV2 71 | 20 | 200 |
| SKI DV2 35 | 350 | 10000 |
| SKI DV2 33 | 4000 | >10000 |
| SKI DV 103 | 10000 | >10000 |

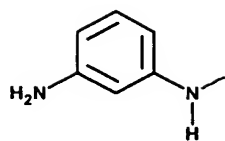
Figure 17

A

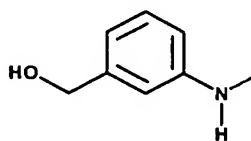


6-(2,6-dichlorophenyl)-8-methylpyrido[2,3-d]pyrimidin-7(8H)-one

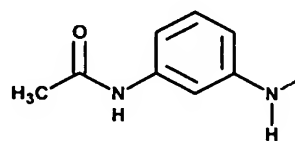
B



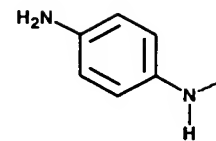
SKI DV 2-43



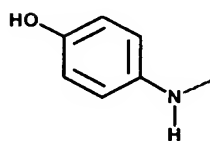
PD166326



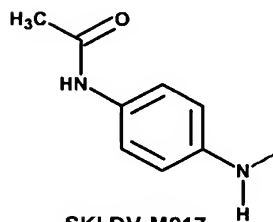
SKI DV-M016



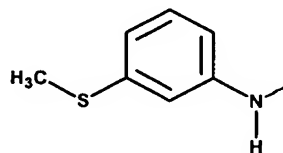
SKI DV 1-10



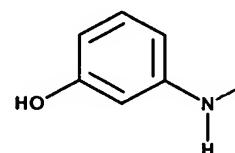
SKI DV 2-47



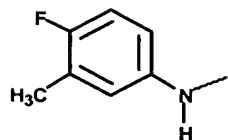
SKI DV-M017



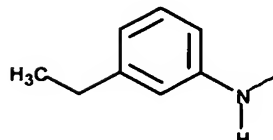
PD173955



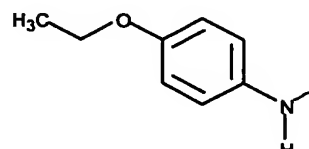
SKI DV 2-89



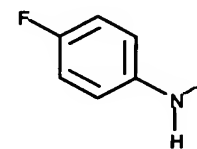
PD180970



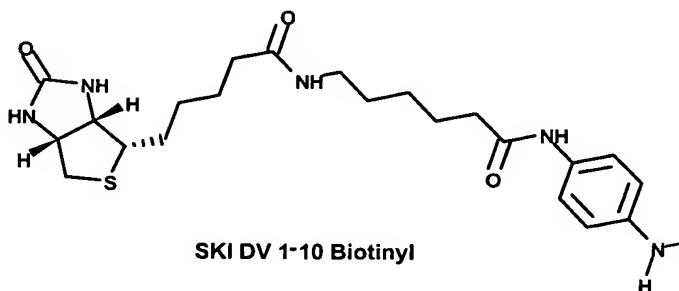
SKI DV 2 87



PD173958



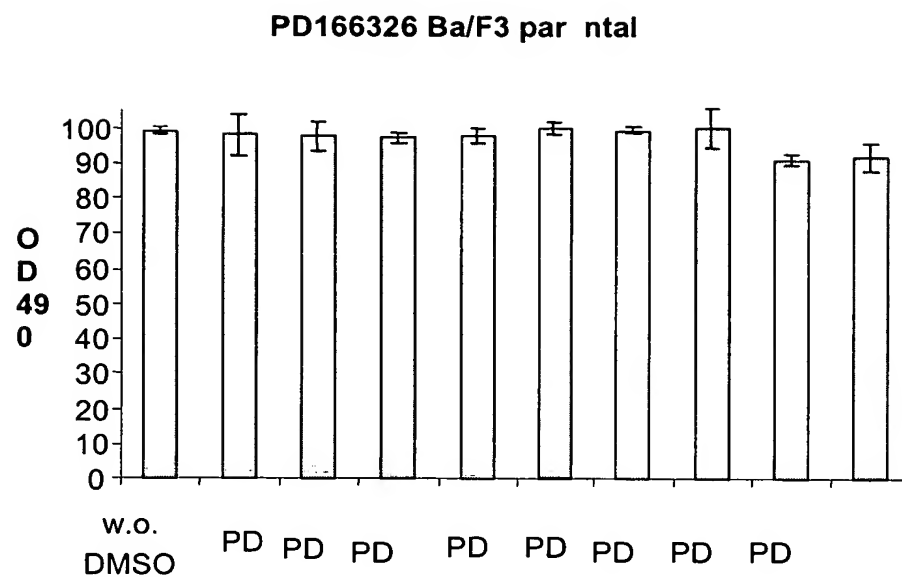
PD173956



SKI DV 1-10 Biotinyl

Figure 18

A



B

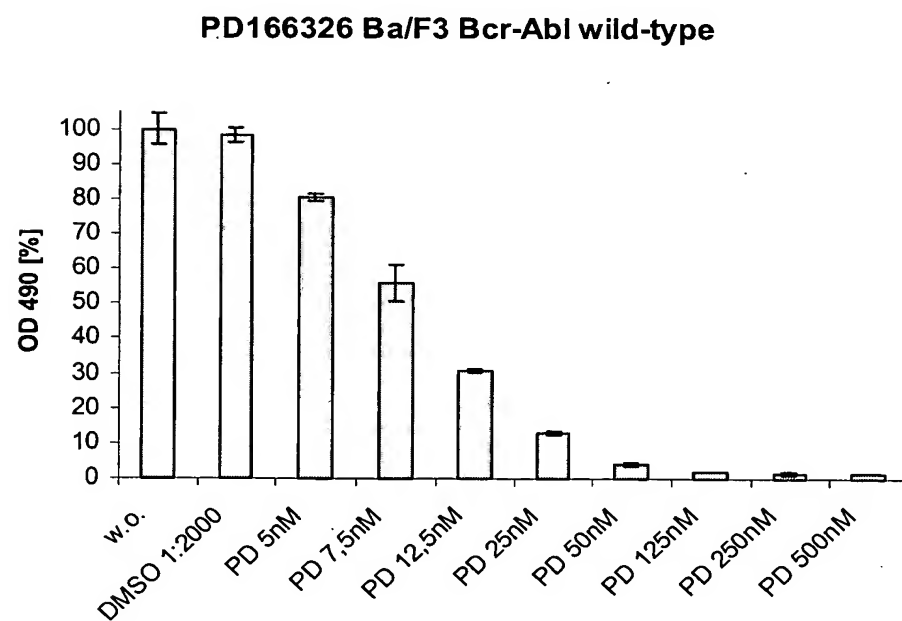
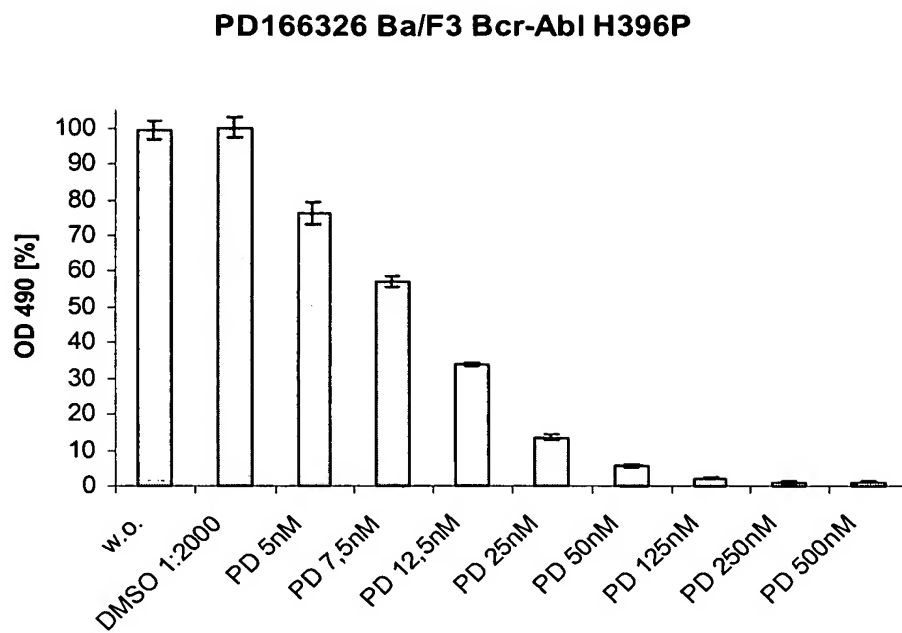


Figure 19A

C



D

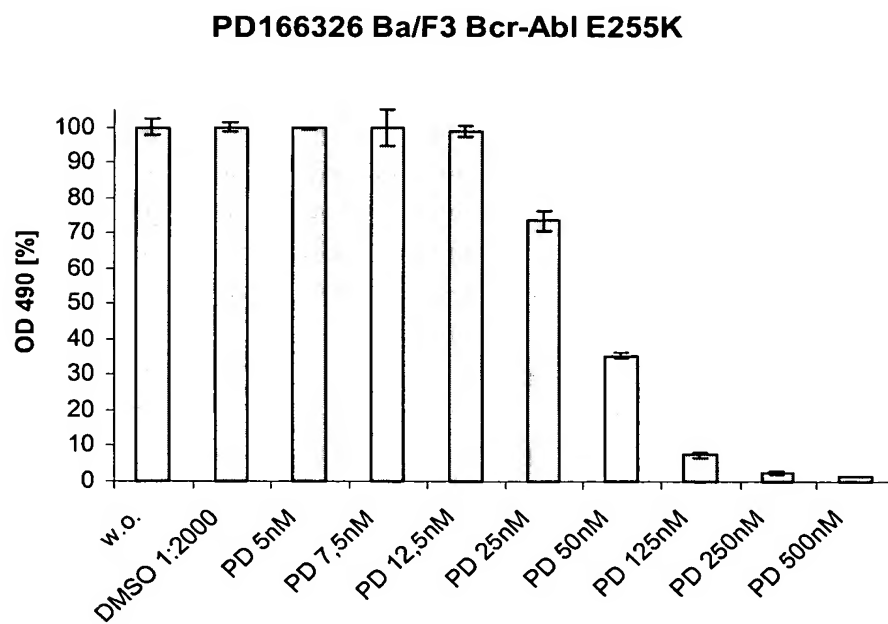
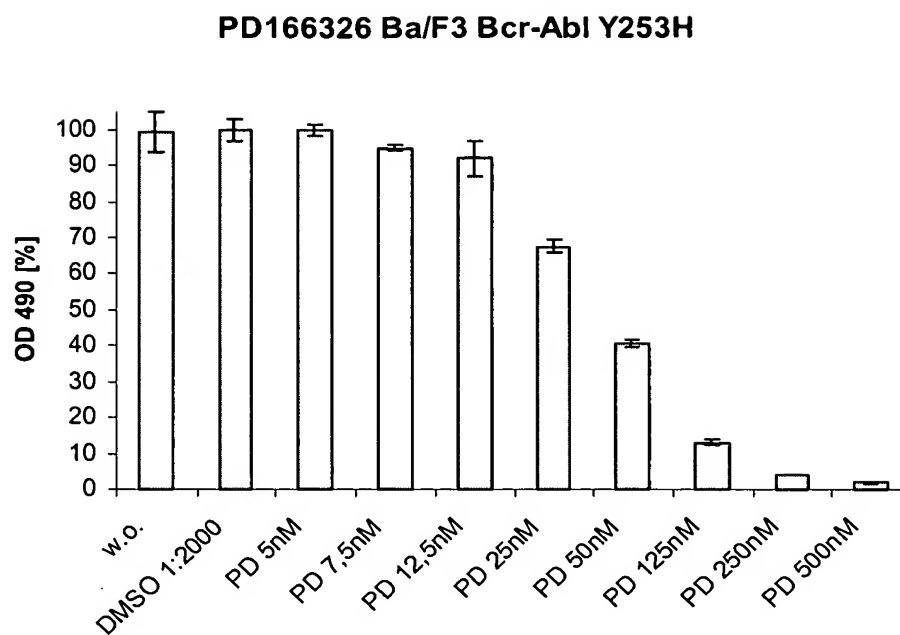


Figure 19B

E



F

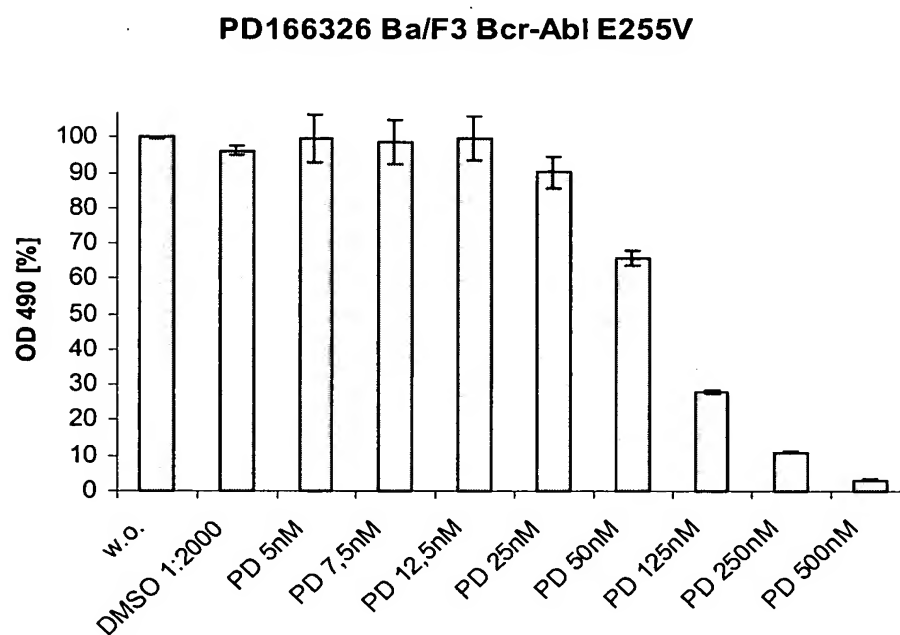


Figure 19C

G

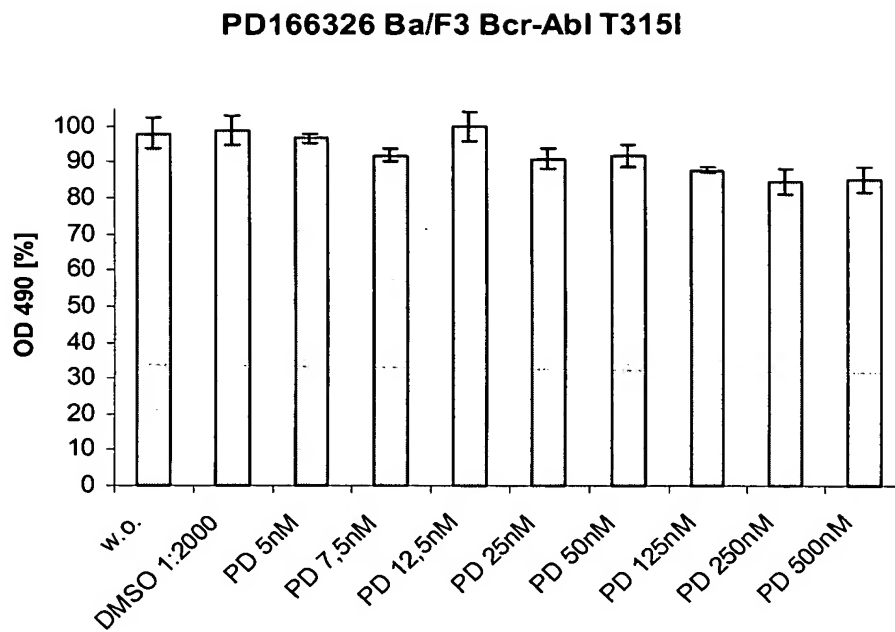
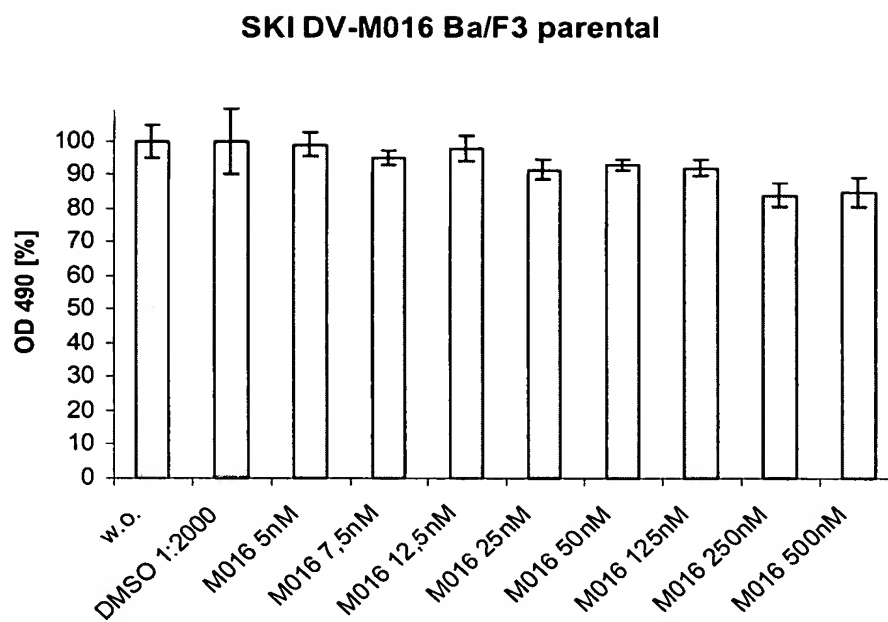


Figure 19D

A



B

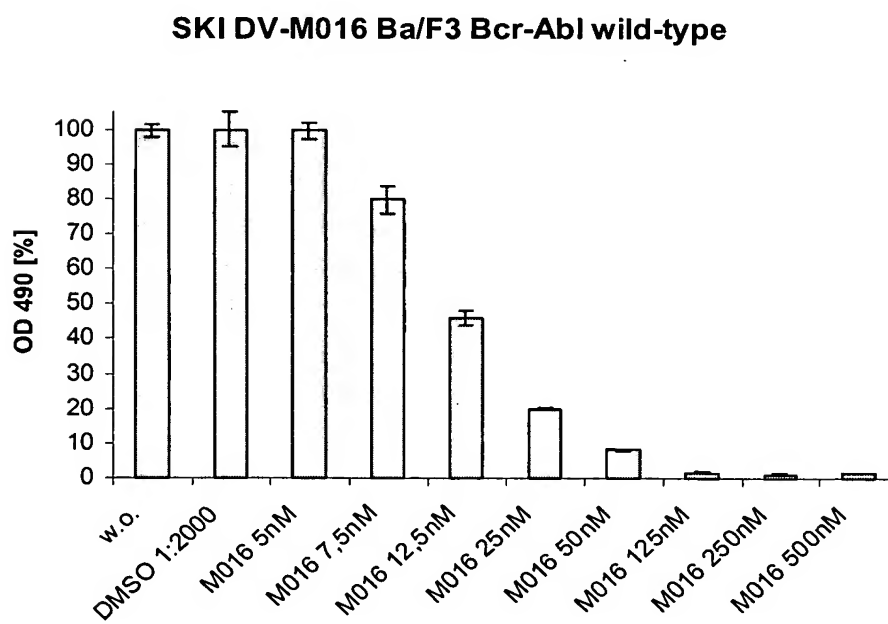
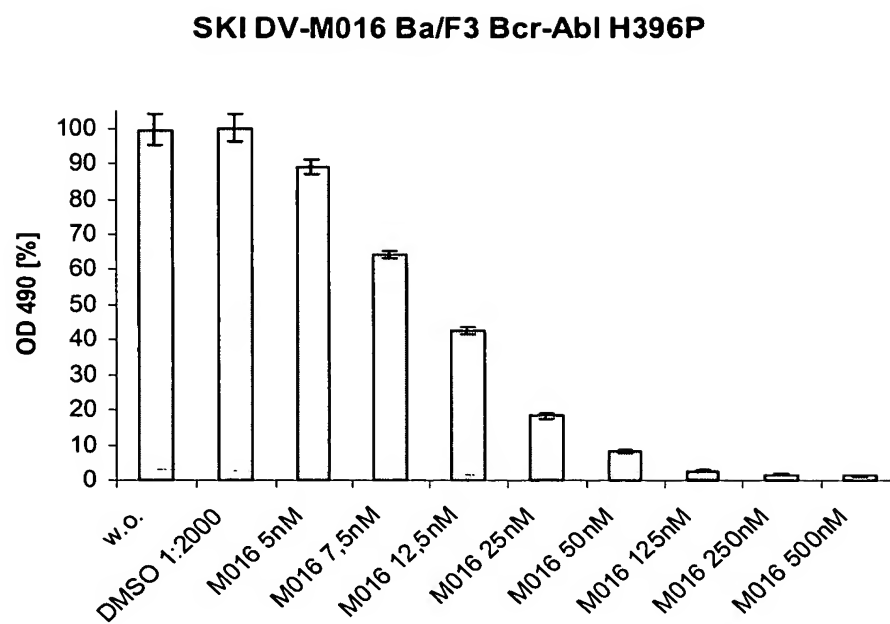


Figure 20A

C



D

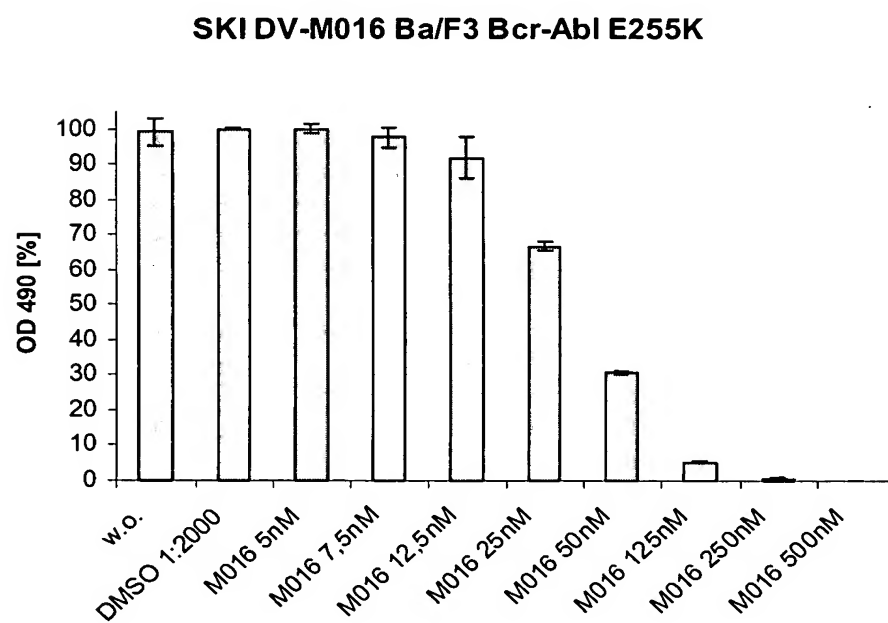
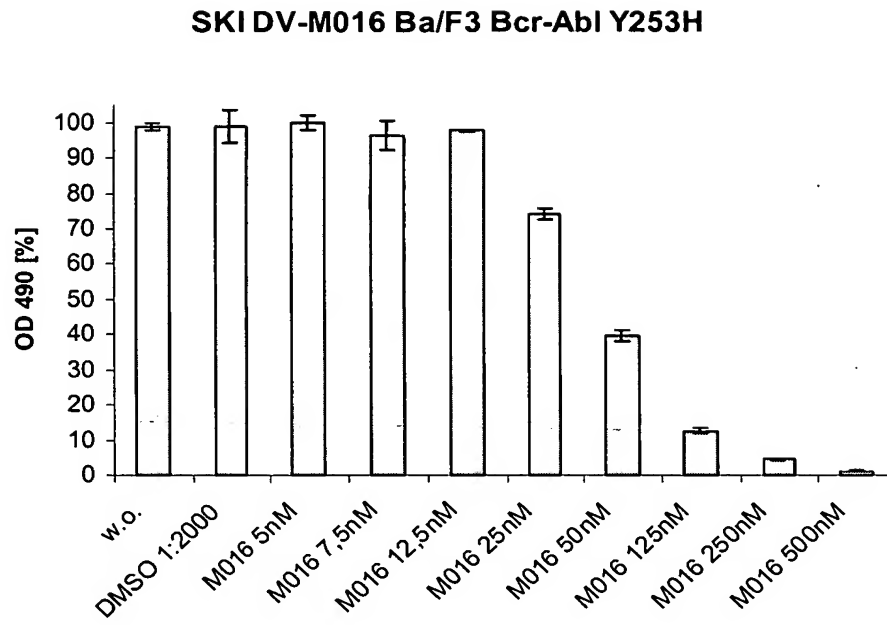


Figure 20B

E



F

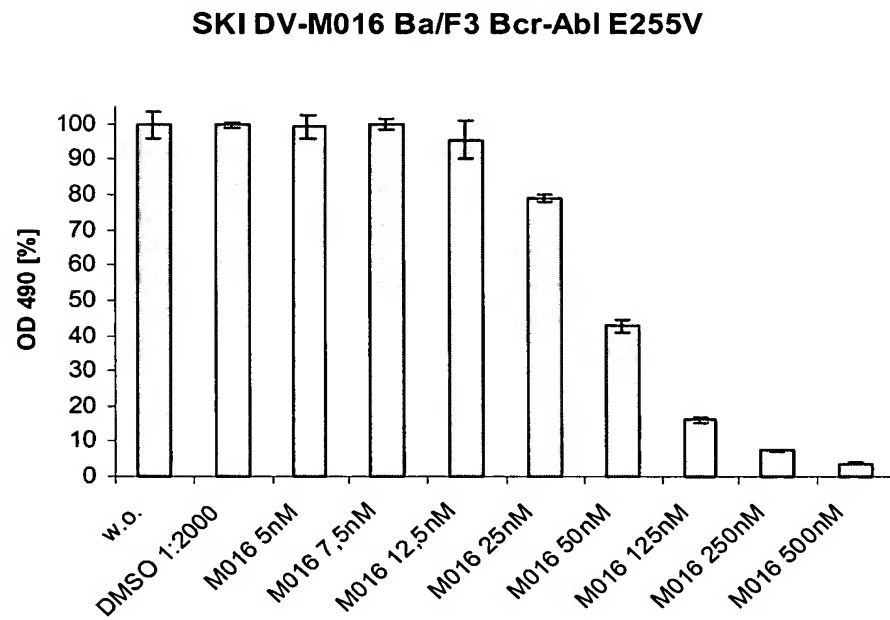


Figure 20C

G

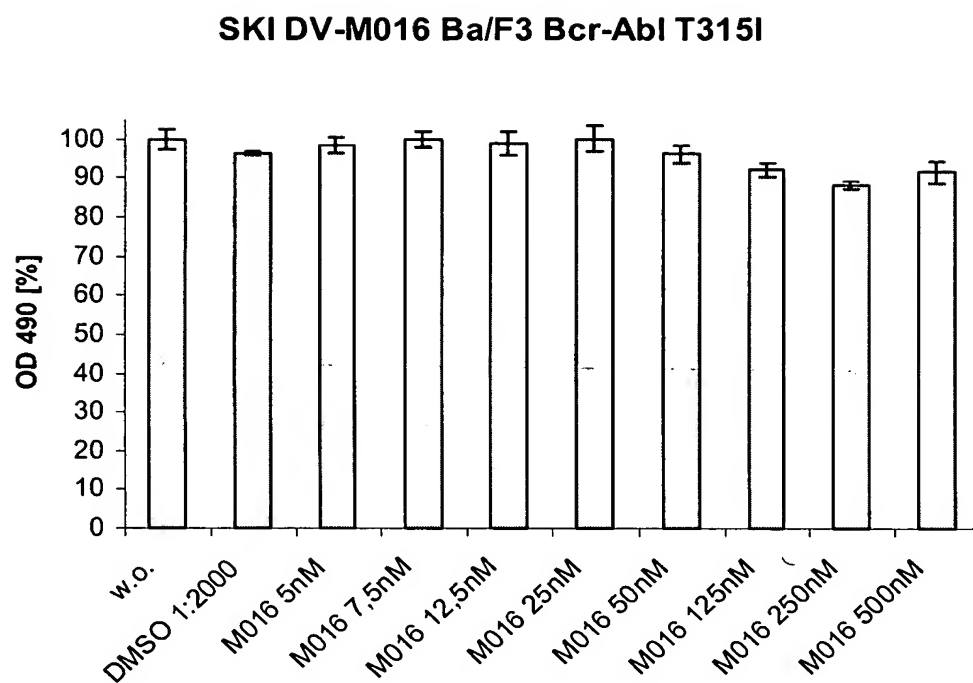
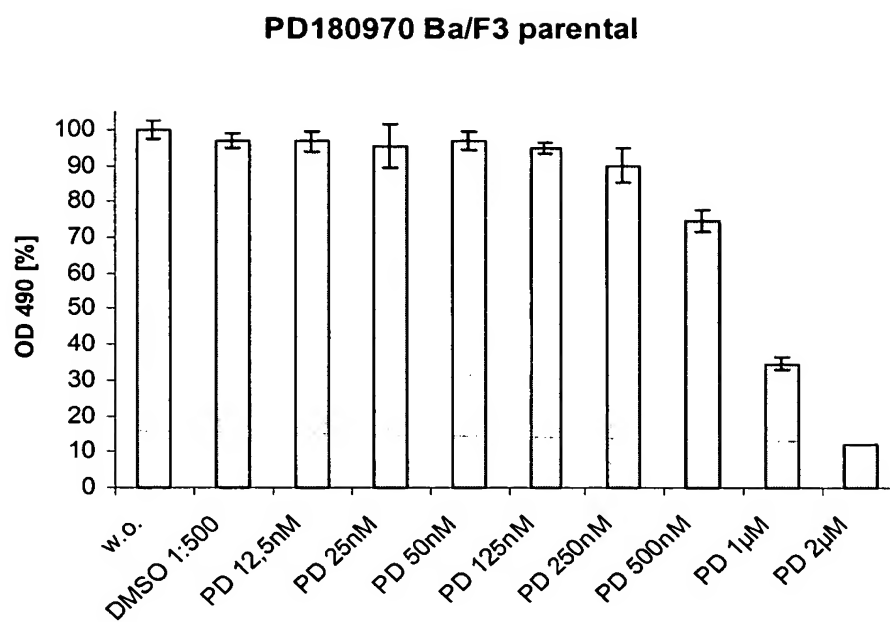


Figure 20D

A



B

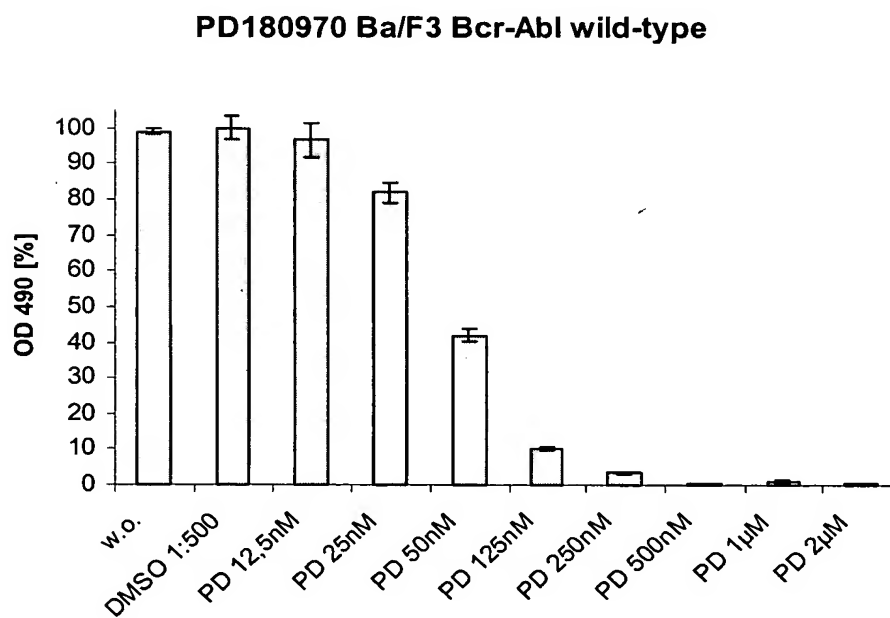
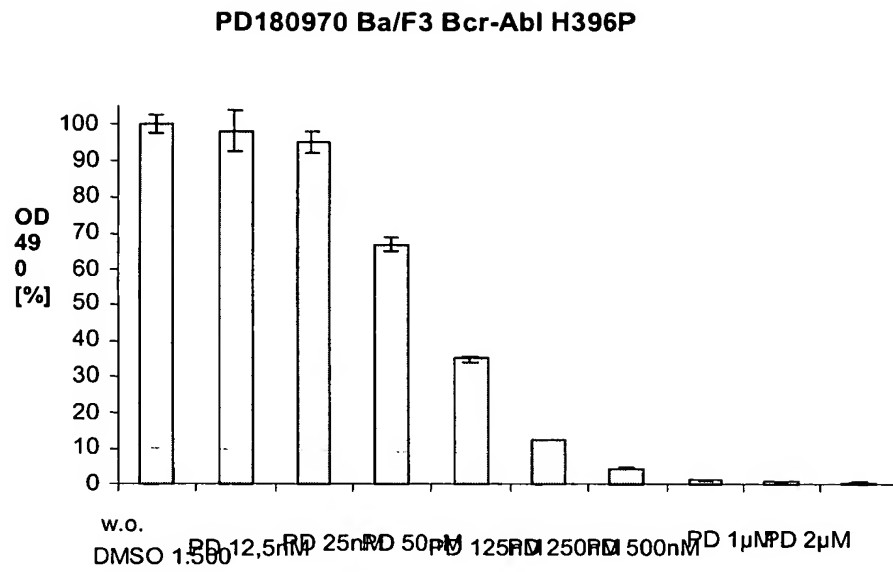


Figure 21A

C



D

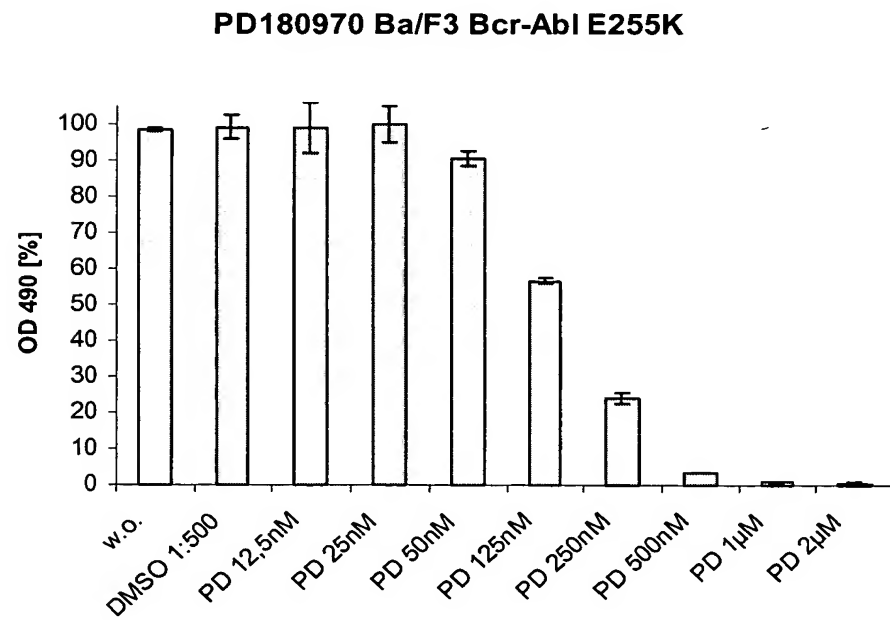
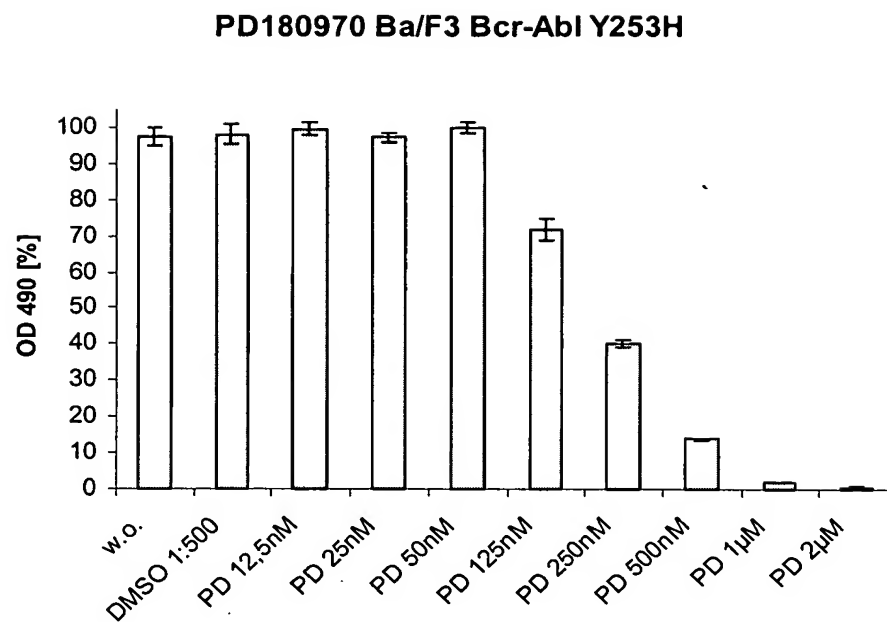


Figure 21B

E



F

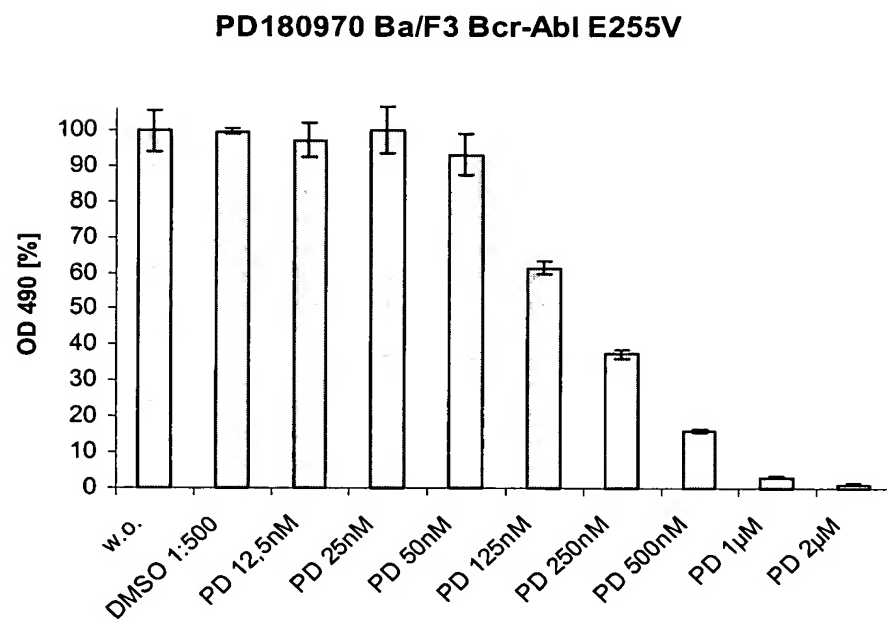


Figure 21C

G

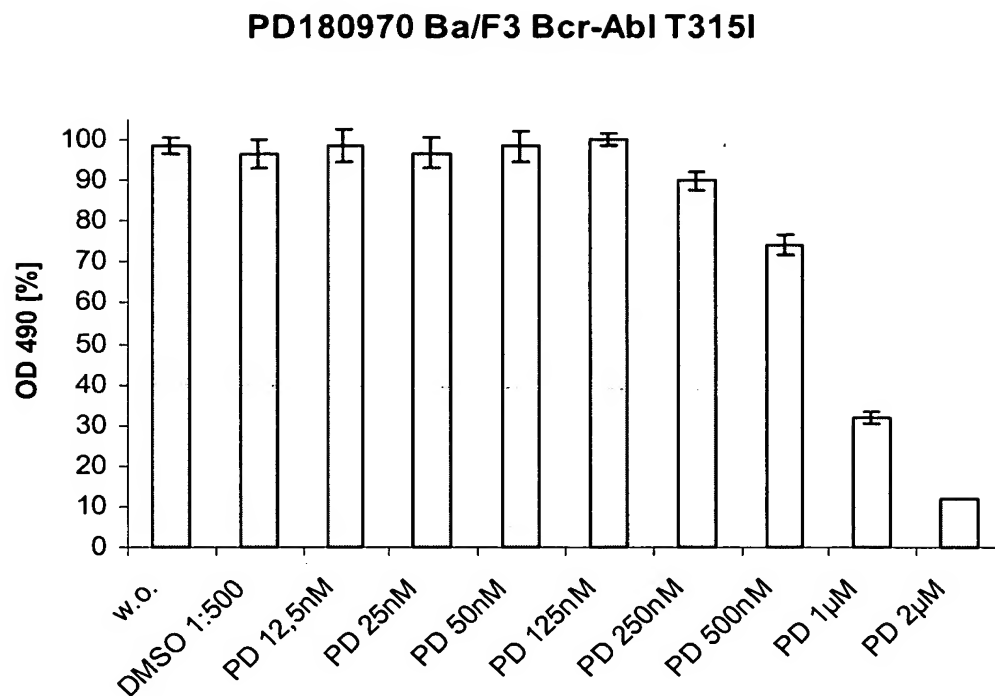


Figure 21D

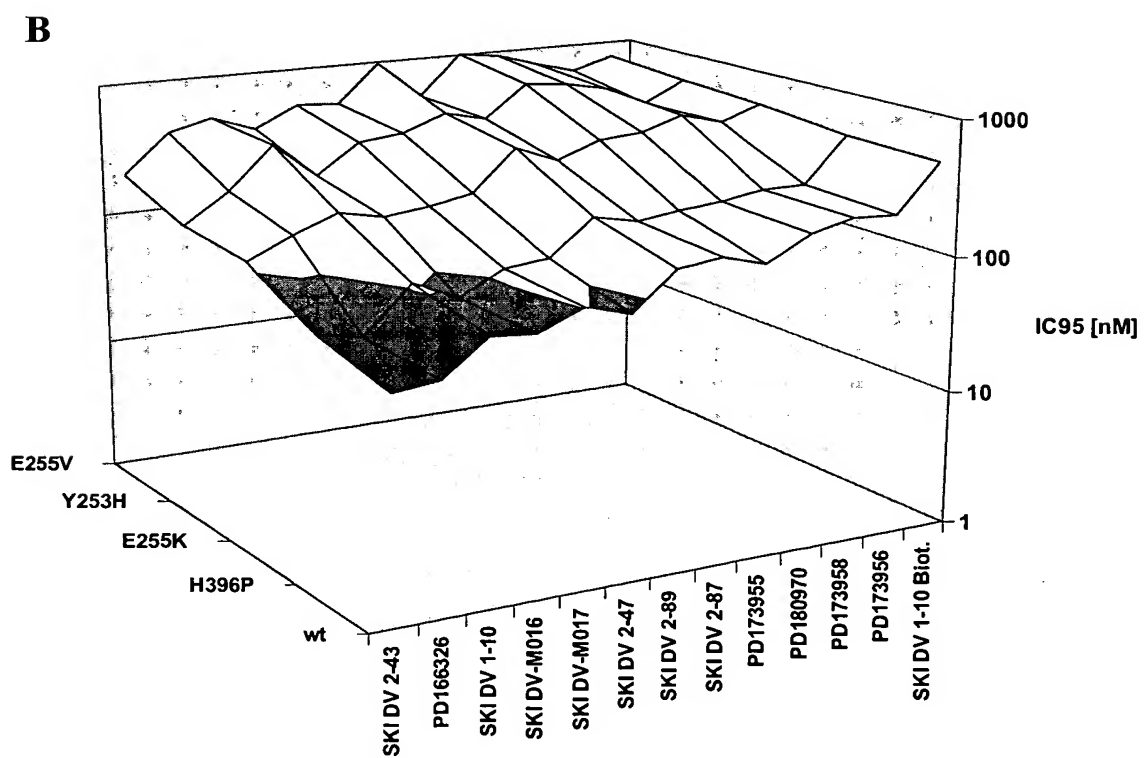
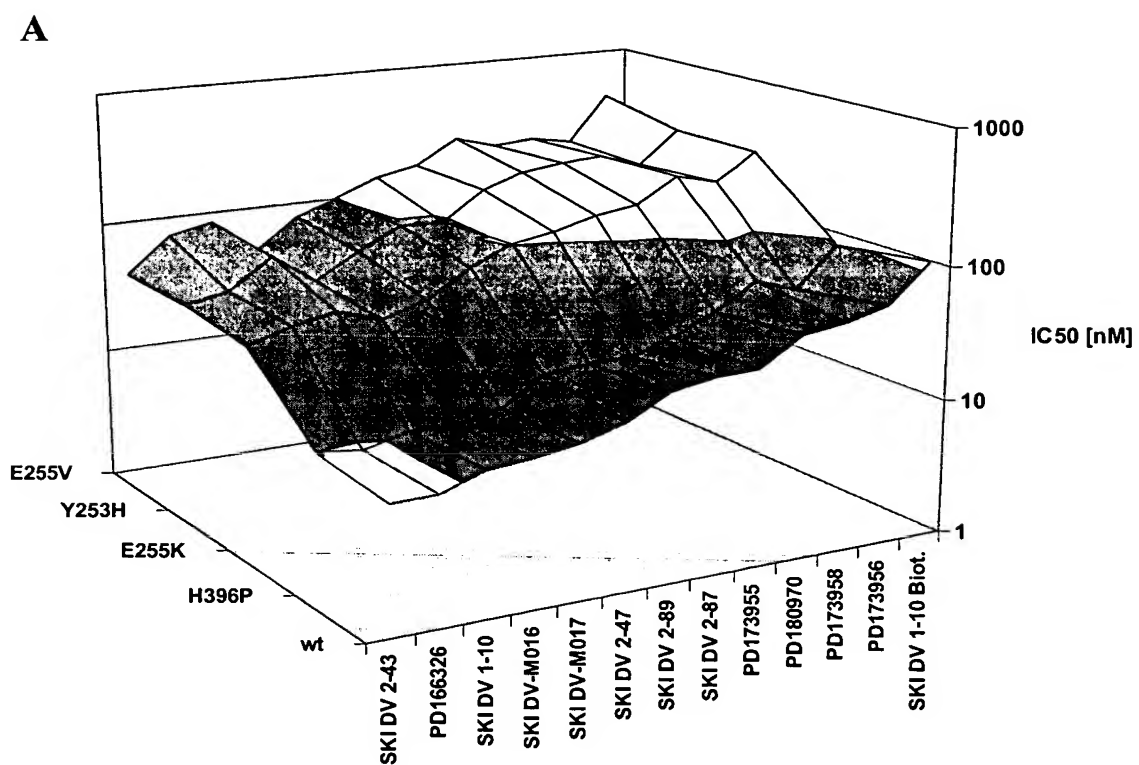


Figure 22

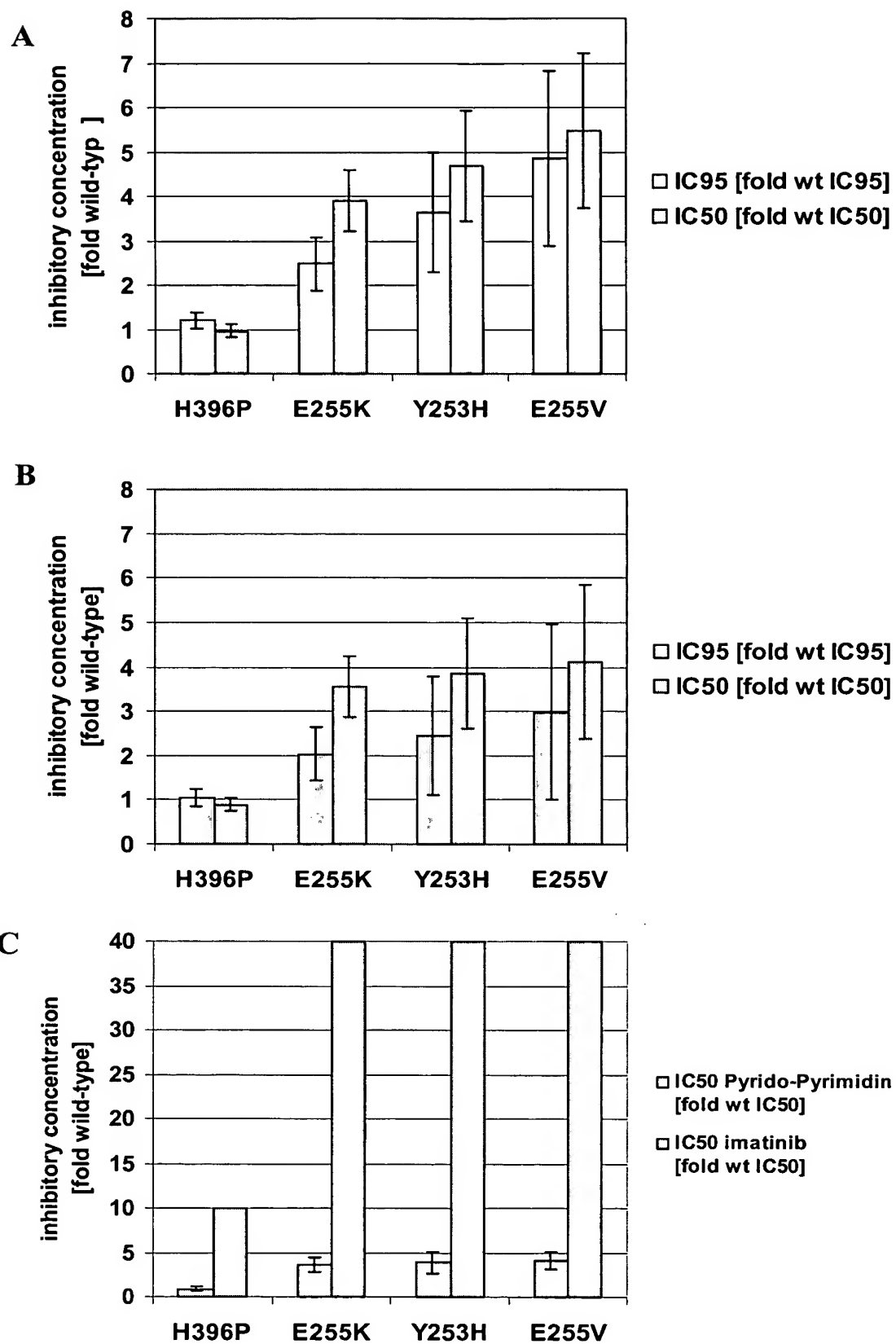
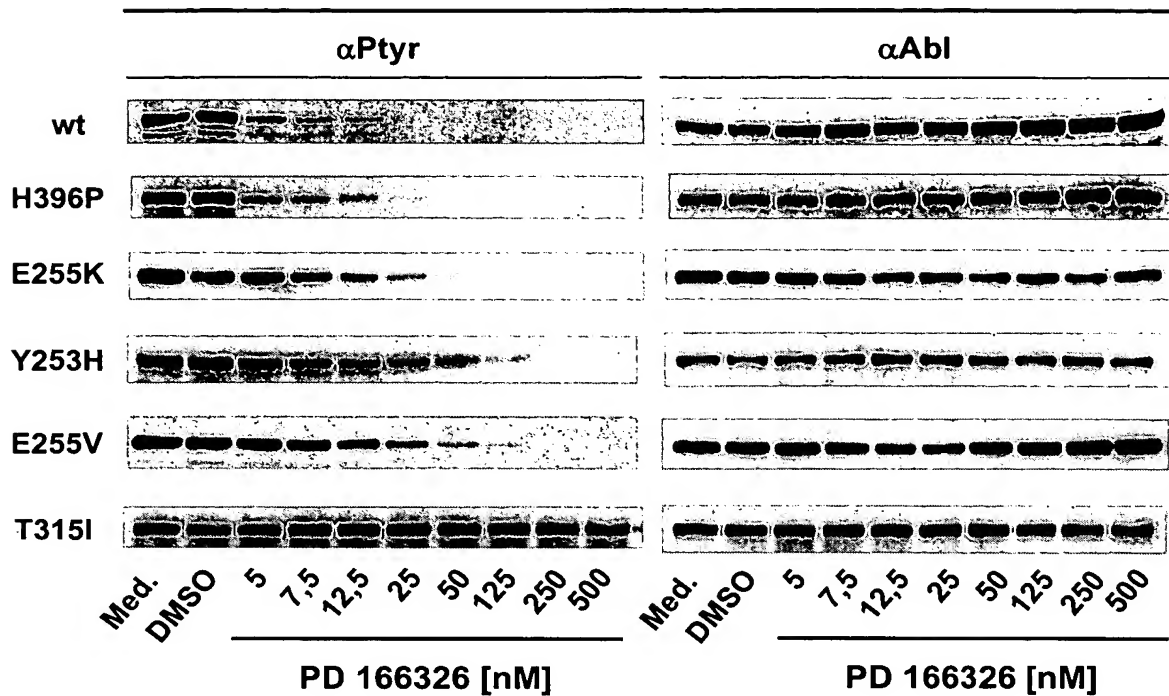
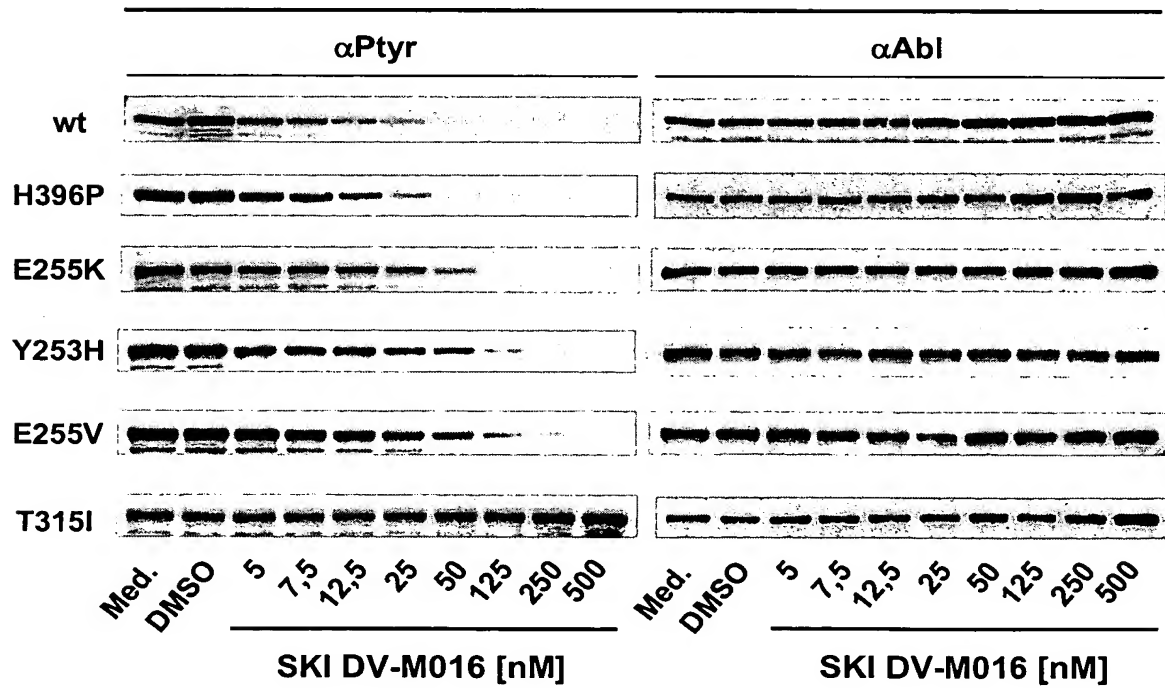


Figure 23

A**Bcr-Abl****B****Bcr-Abl****Figure 24**

C

Bcr-Abl

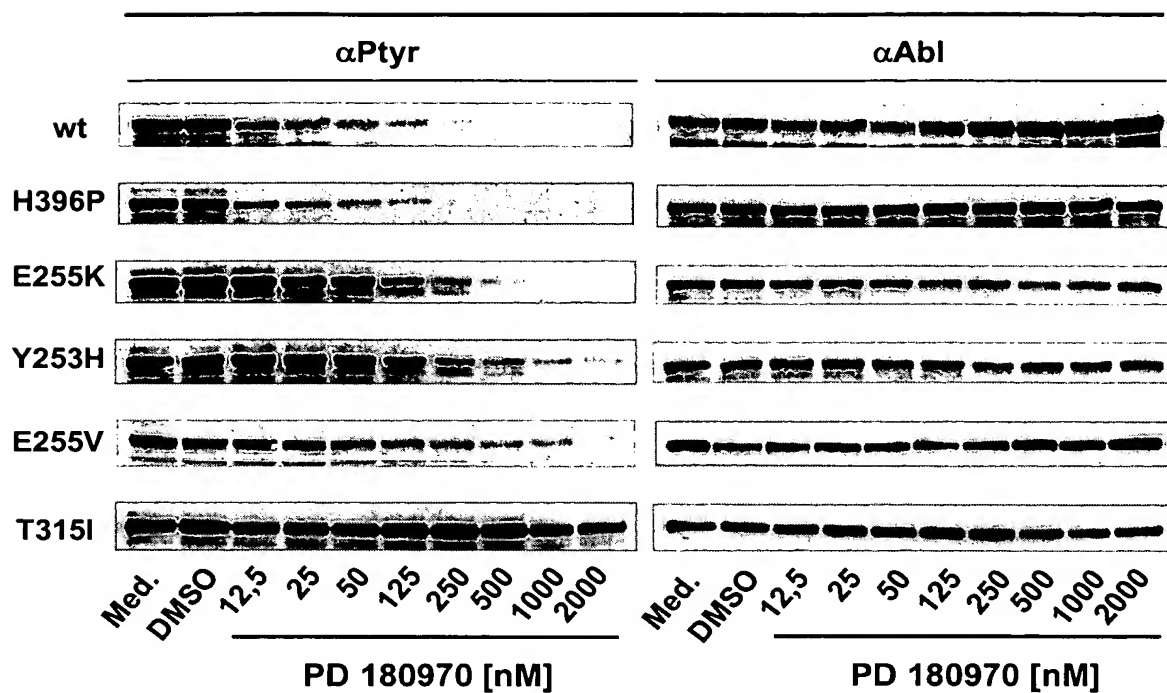
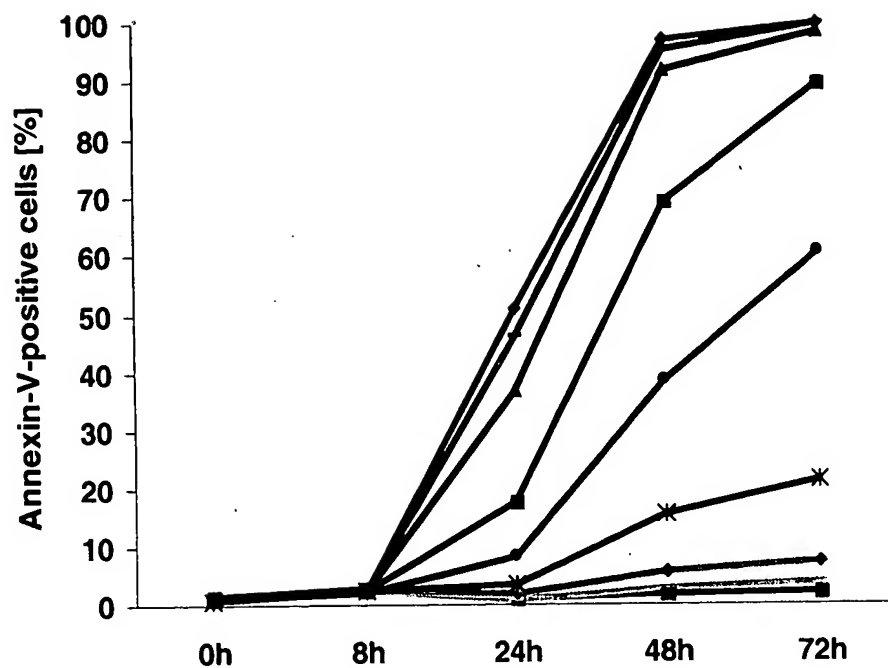


Figure 24B

A



B

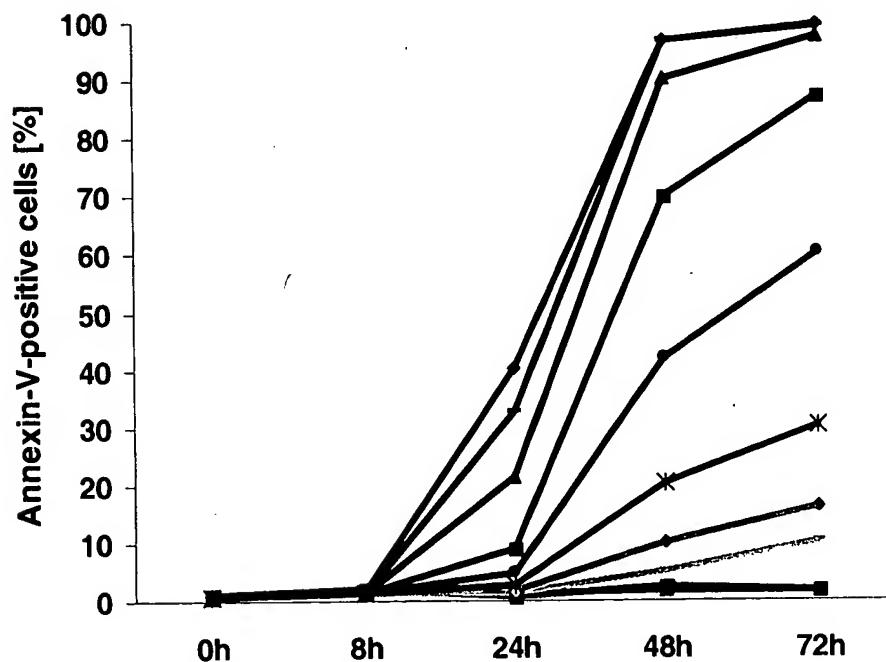
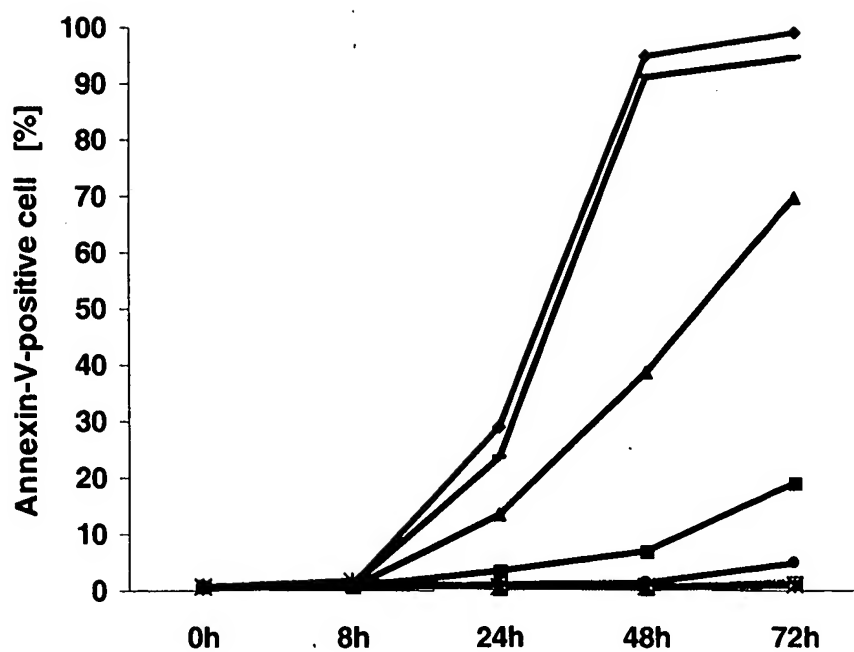


Figure 25A

- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM

C



D

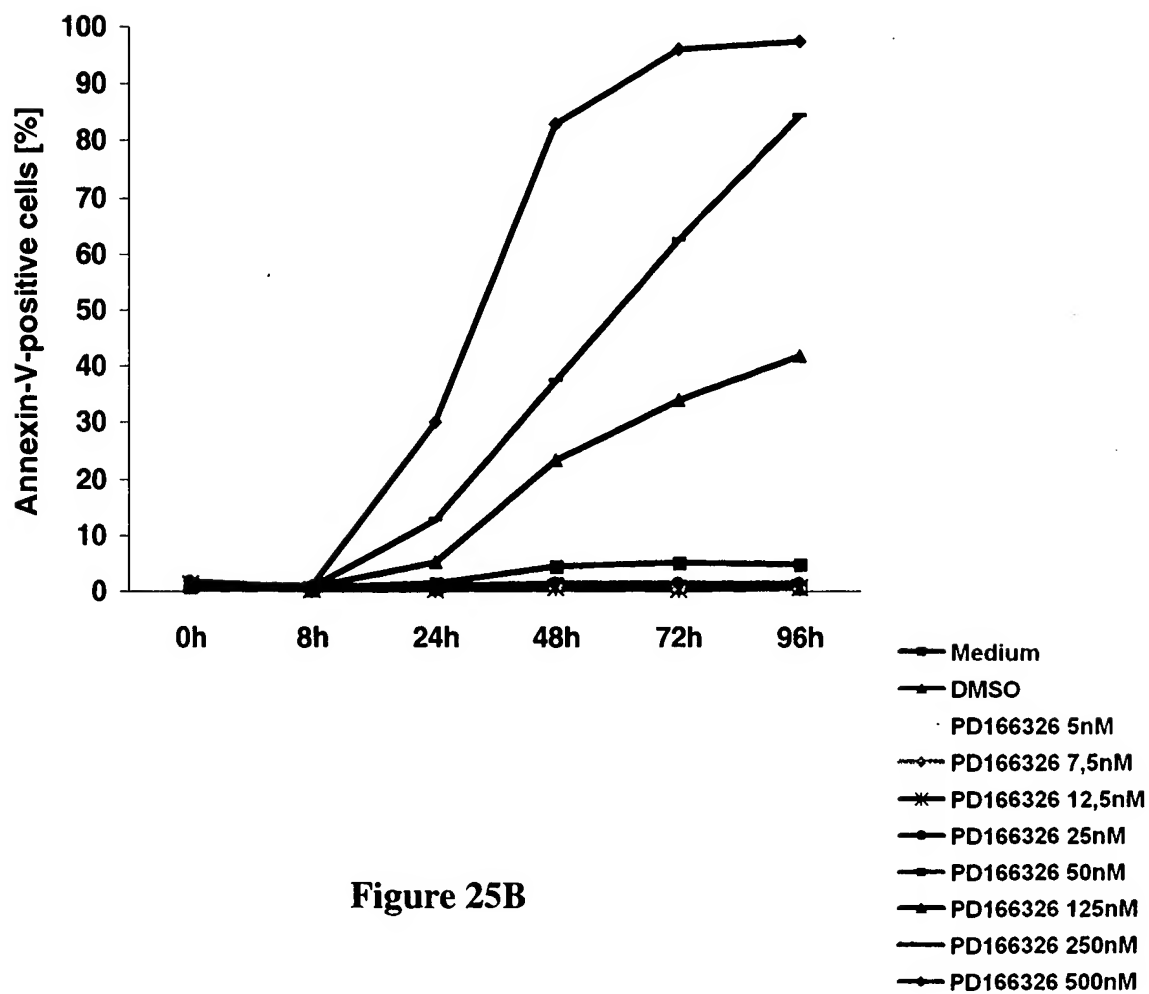
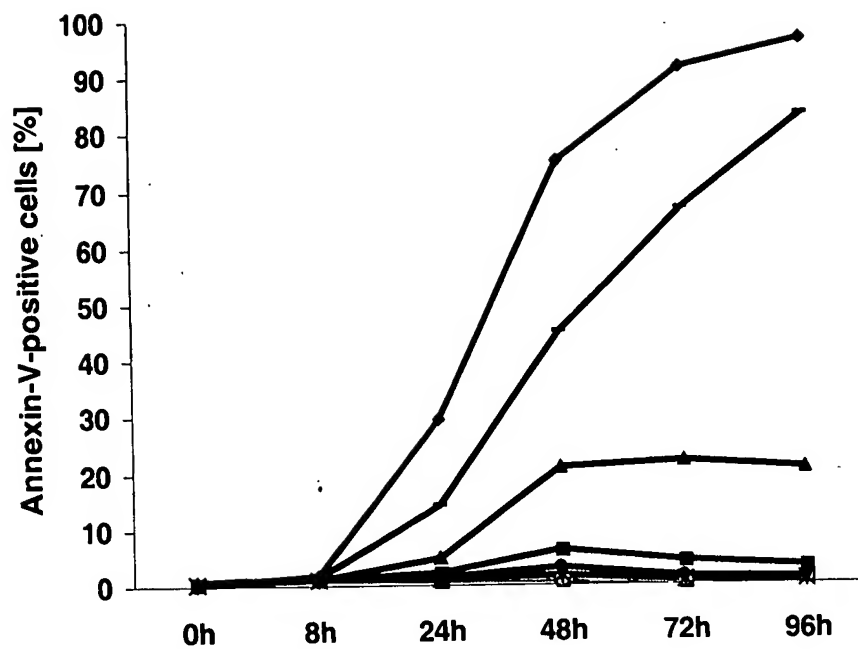
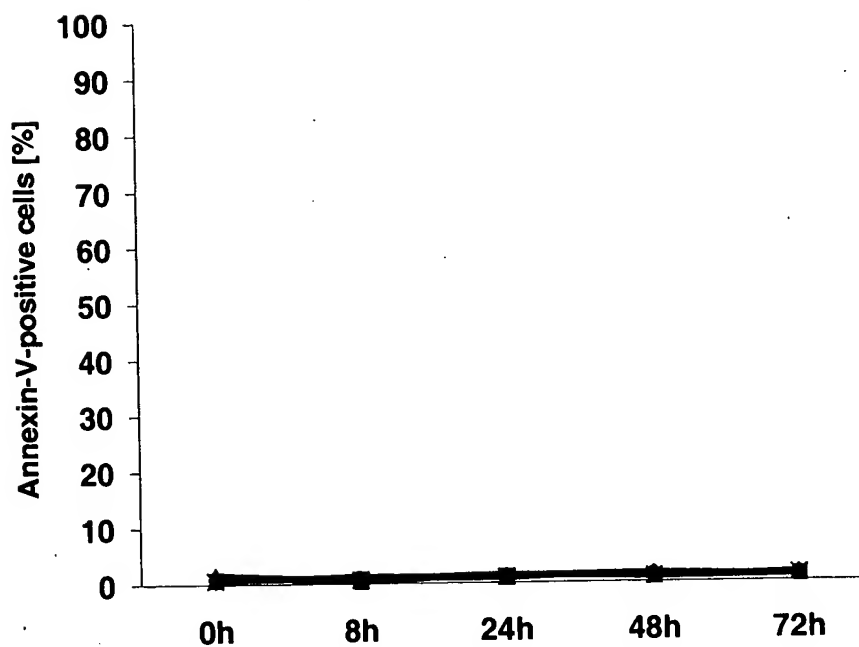


Figure 25B

E



F



- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM

Figure 25C

G

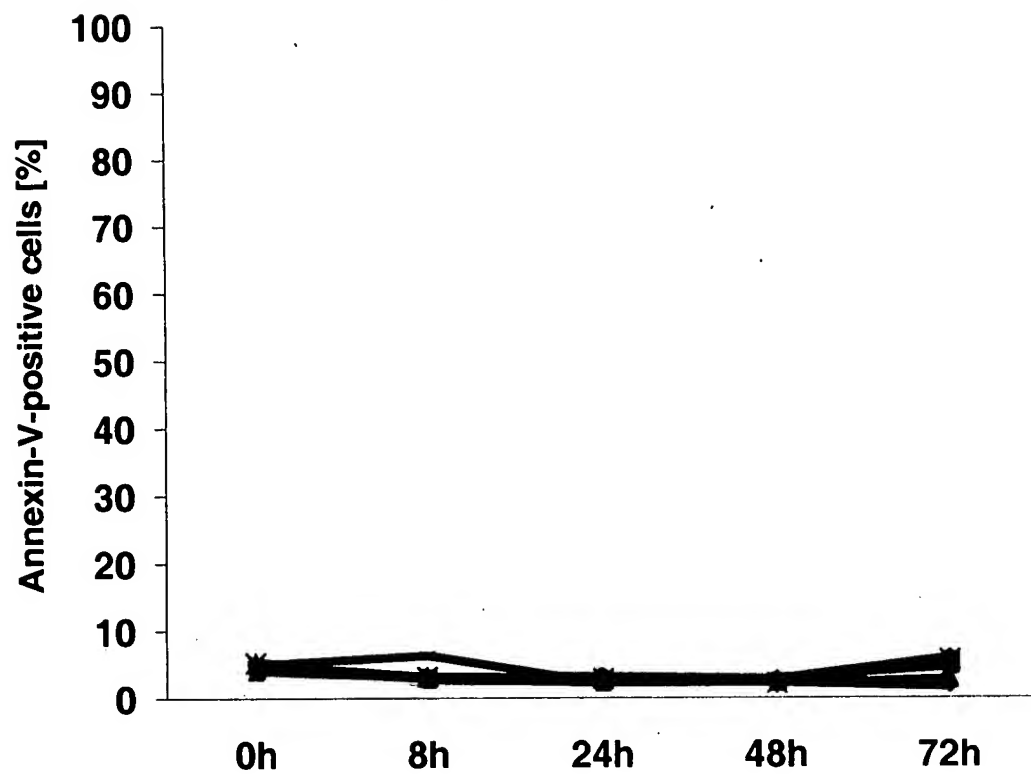


Figure 25D

- Medium
- DMSO
- PD166326 5nM
- PD166326 7,5nM
- PD166326 12,5nM
- PD166326 25nM
- PD166326 50nM
- PD166326 125nM
- PD166326 250nM
- PD166326 500nM

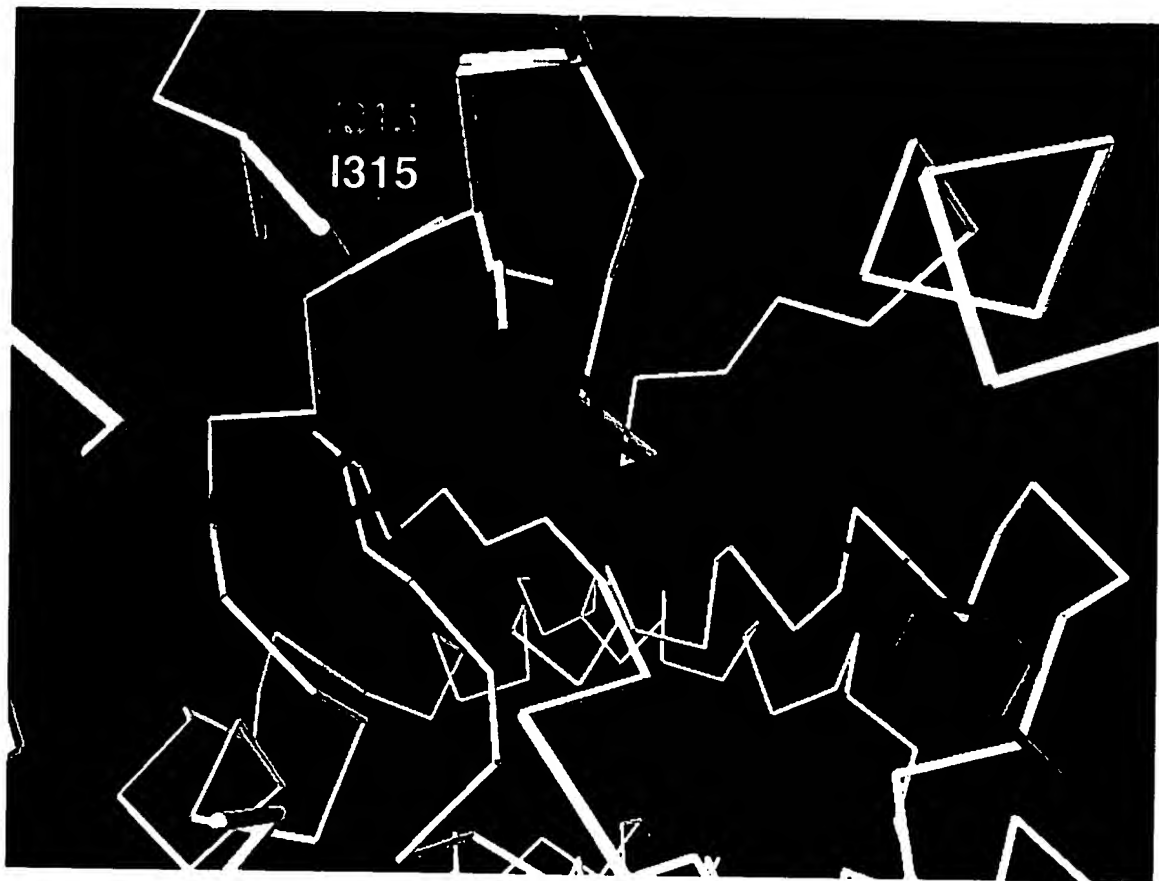


Figure 26

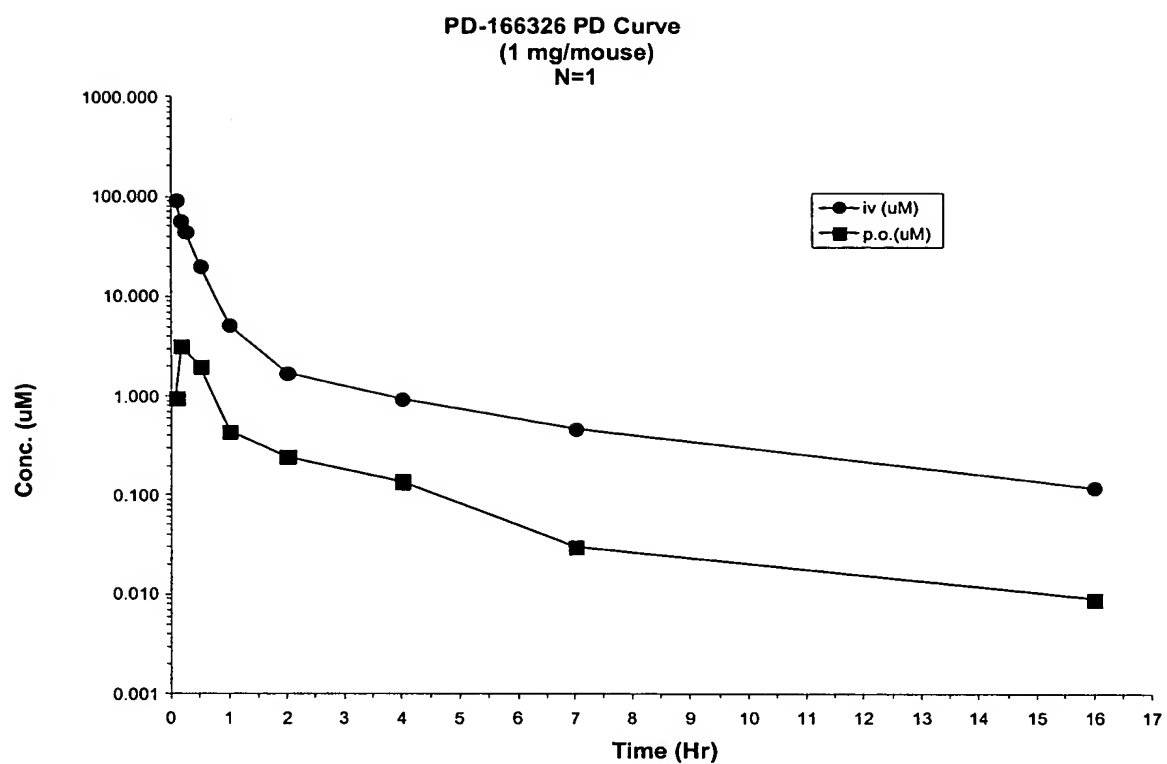


Figure 27

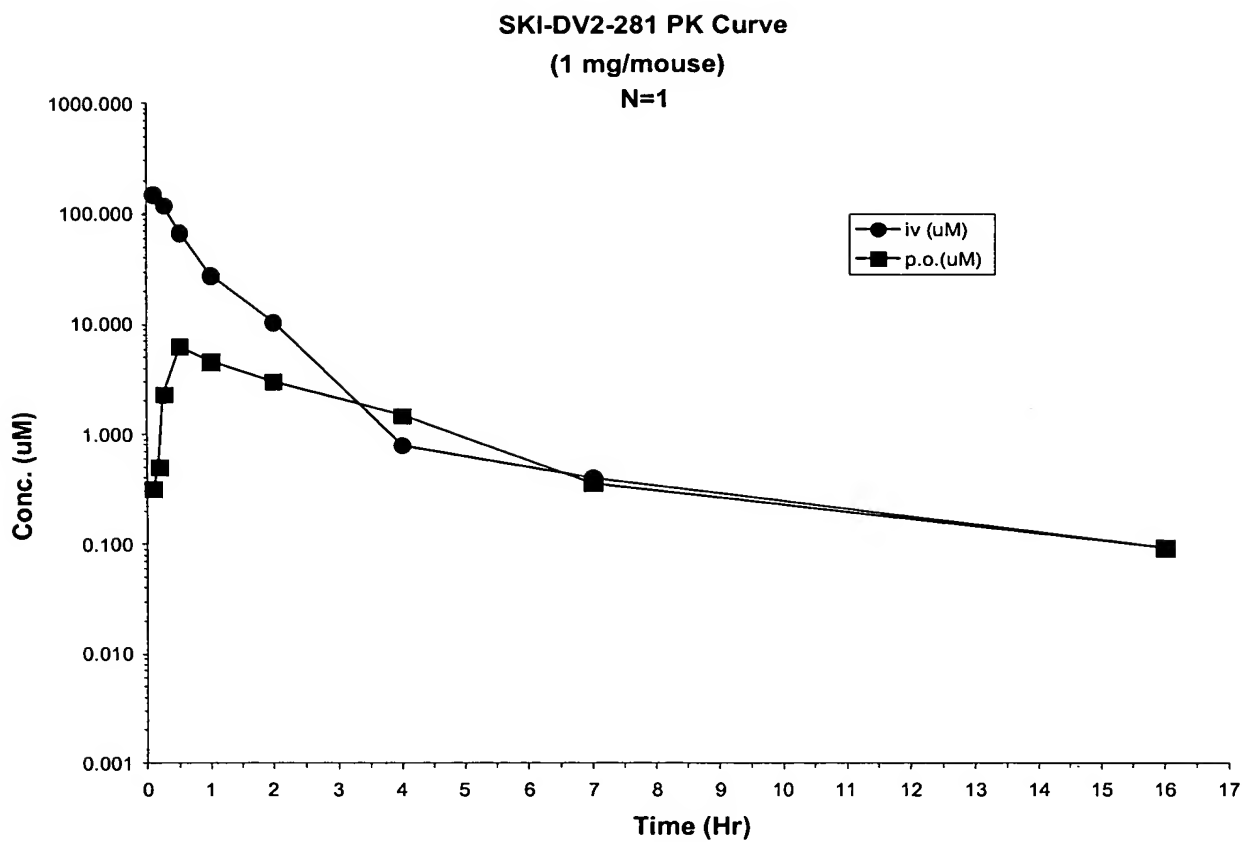


Figure 28

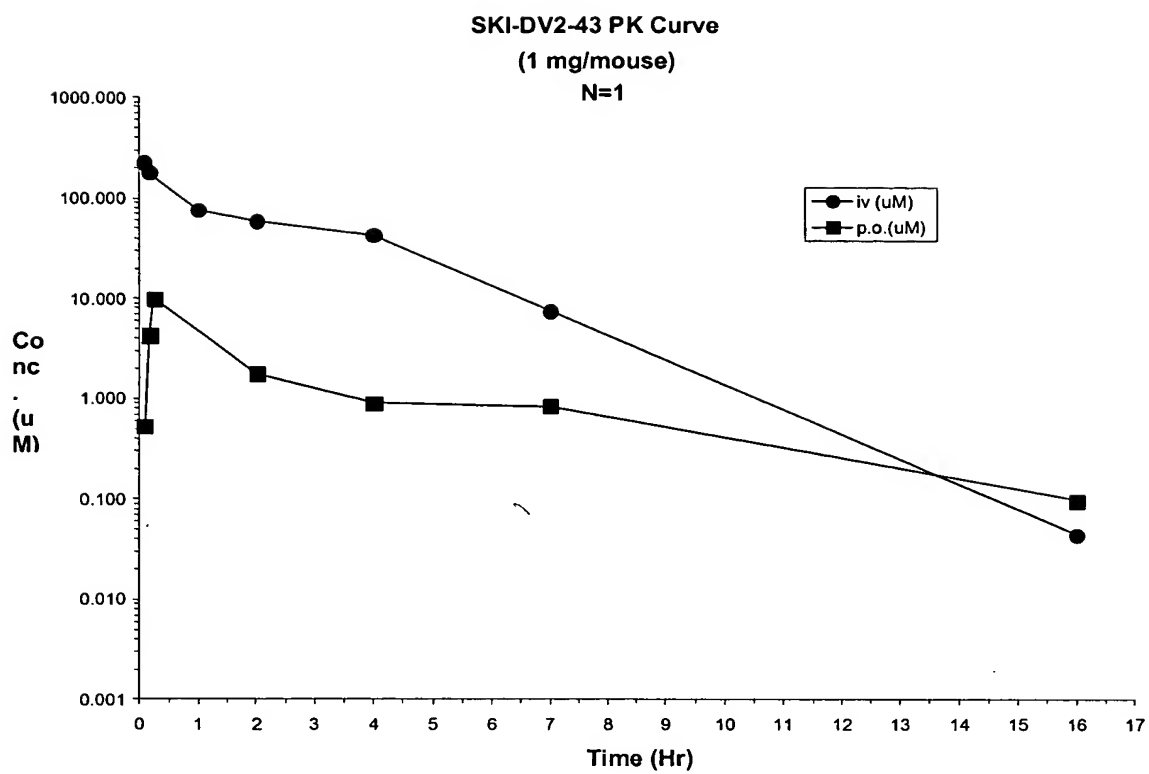


Figure 29

**Comparison of 6 of Most Inhibitory Pyrido- Pyrimidines to Bcr-Abl
in Inhibiting Recombinant Abl & Src Kinases *in vitro***

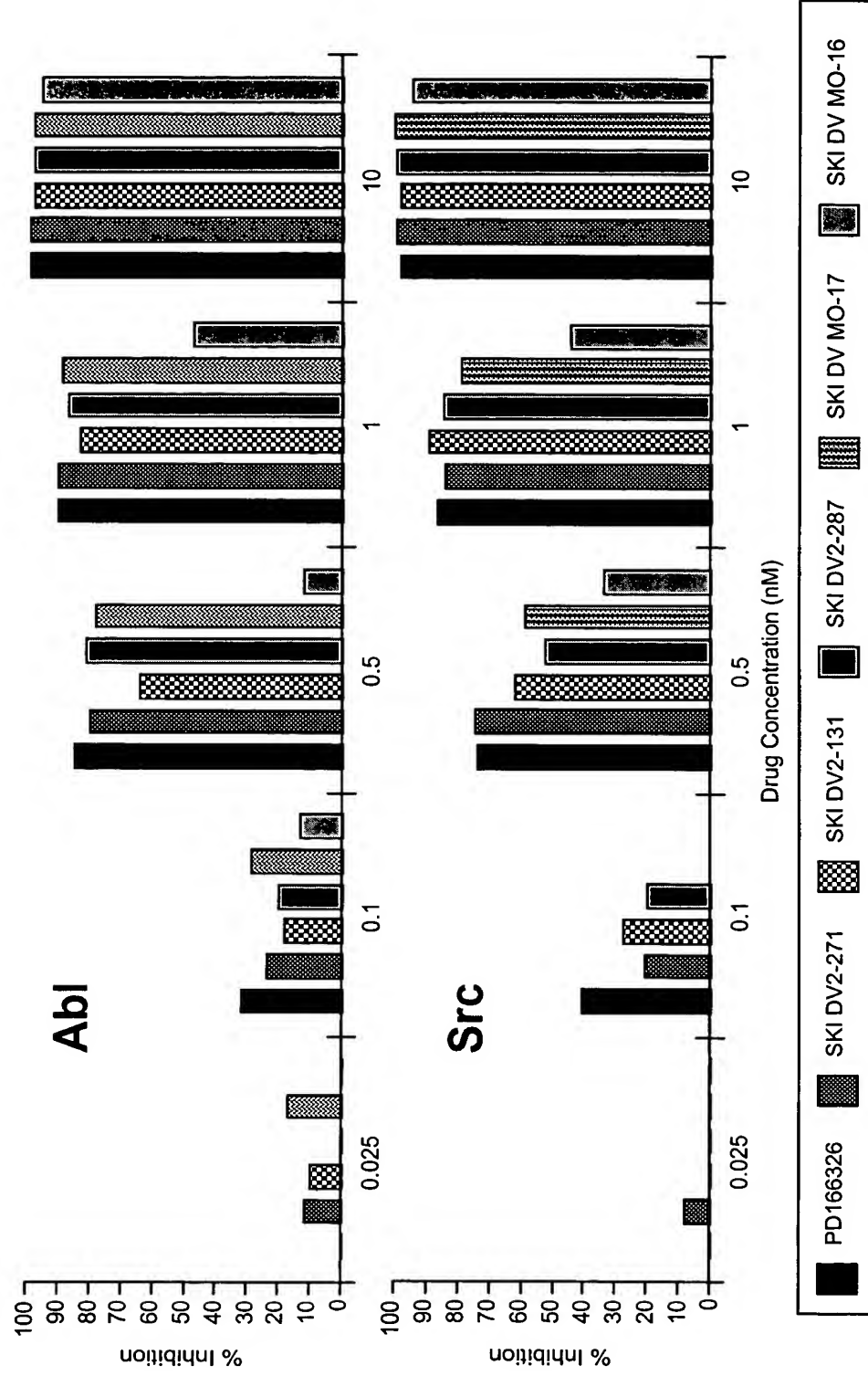


Figure 30

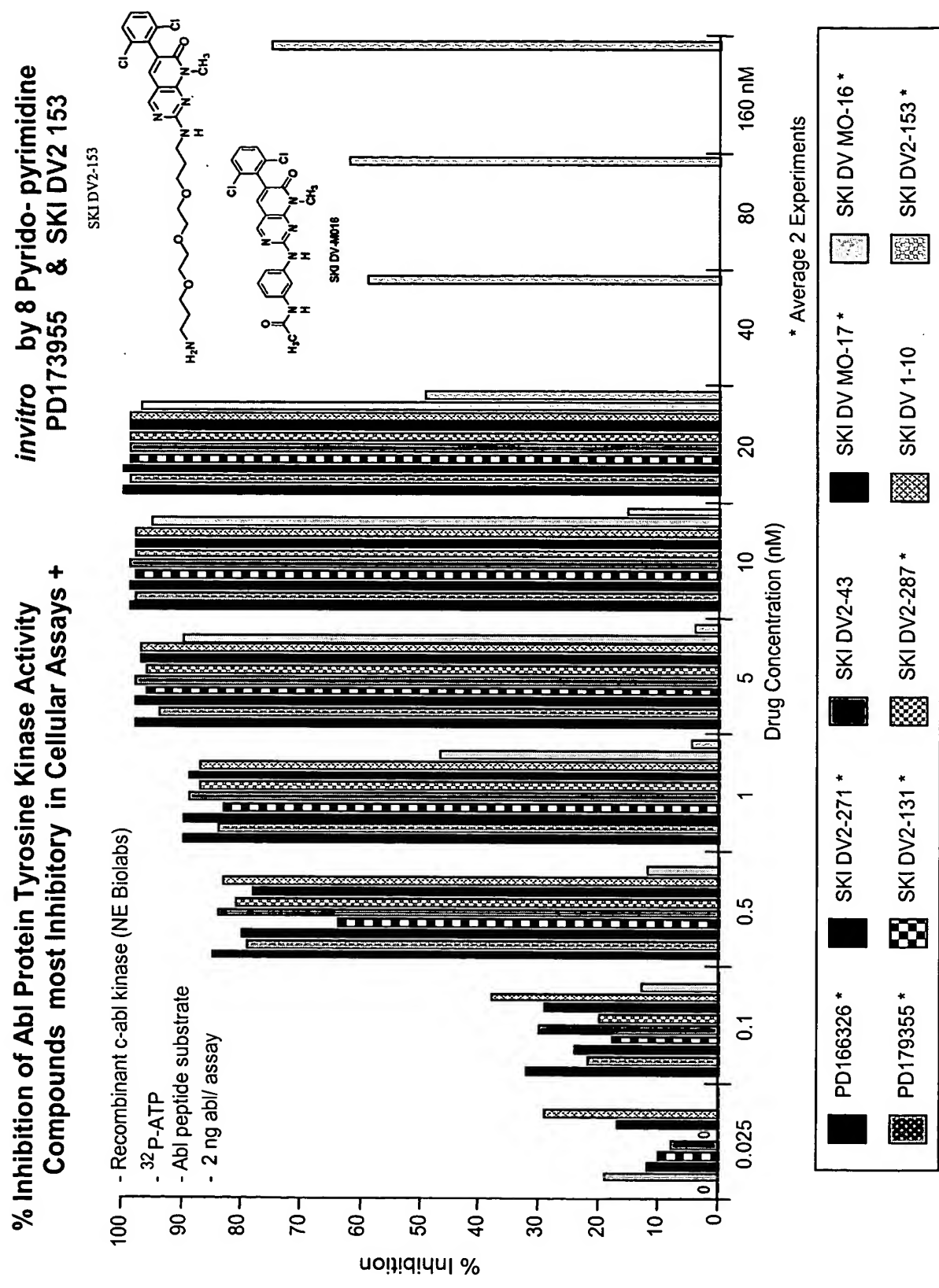


Figure 31